V31
#10

British Journal of Anaesthesia

JOINT EDITORS:

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Volume XXXI No. 10 October 1959

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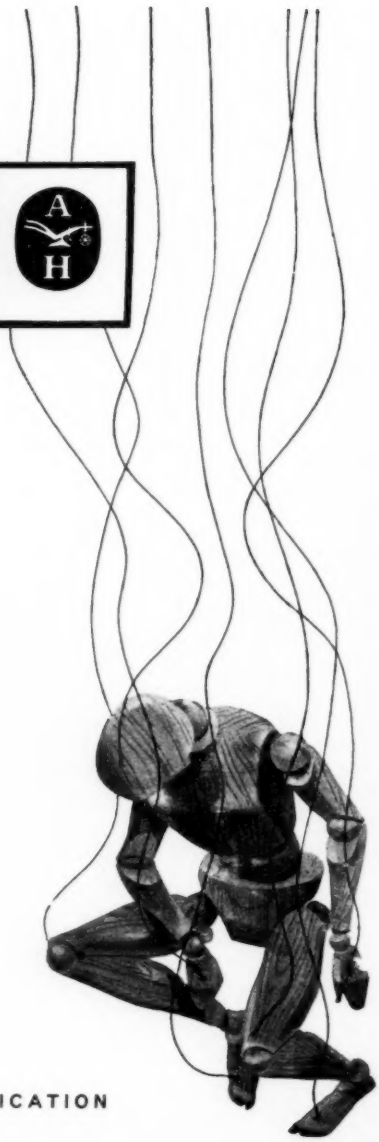

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BRITISH JOURNAL OF ANAESTHESIA

VOL. XXXI, No. 10 OCTOBER 1959

EDITORIAL

IS CLINICAL JUDGMENT ENOUGH?

THOSE giving anaesthesia in Britain are for the most part experienced practitioners in the specialty. Because of their accumulated clinical experience they are very successful in estimating the state of the patient at any given time during the course of the operation. Almost to the exclusion of all other aids, they rely on this state to determine when to deepen or lighten the anaesthesia, when to increase the dose or when to lessen it. If the condition of the patient were due to the anaesthetic alone, it would be a good deal easier to make a correct estimation of the situation than it is. However, seeing that this condition is the resultant of numerous factors such as the nature of the complaint, the operation, the operator, the amount and suddenness of haemorrhage, the influence of premedication, the effect of the many different drugs it is now usual to give, this estimation is by no means easy. Is the patient merely asleep or anaesthetized to the point of depression of all his functions? Is his hypotension the result of drugs or other factors? Are we sure that although he shows no cyanosis the pulmonary ventilation is adequate?

Most anaesthetists, if they are supplied with some rough and ready apparatus giving more or less anaesthetic vapour, are apparently quite satisfied and neither know nor are concerned with the actual percentage being administered. Clinical experience often compensates for the lack of more refined methods—but is this really satisfactory?

There can be no doubt that the time and money being expended on the search for reasonably accurate and objective monitors of the respiratory and cardiovascular function during anaesthesia will increase the safety and comfort of our patients.

In this issue two papers, one on the pharmacology of halothane in man by Payne and his colleagues and the other by Parkhouse and Simpson on a restatement of anaesthetic principles, show the desirability of a less haphazard and nicer approach by the use of accurate inhalers. These, to us, seem valuable steps in the right direction.

Brit J. Anaesth. (1959), **31**, 424

THE PHARMACOLOGY OF HALOTHANE IN MAN: A REVIEW

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THE pharmacological activity of halothane (chloro-bromo-tri-fluoro-ethane) was first investigated by Raventós (1956) in animals and this work was later extended by Burn, Epstein, Feigan and Paton (1957). These reports and the first clinical study of Johnstone (1956) have provoked much controversy and stimulated further clinical research in man. It is inevitable that by their nature such studies must be limited in extent and it is the purpose of this paper to consider some of the accumulating data in the light of our own experience of halothane anaesthesia in more than 1,000 patients, under a wide variety of conditions.

As no particular group of patients was excluded from our assessment, experience was gained in both elective and emergency procedures in all branches of surgery, obstetrics and gynaecology. Patients were of both sexes and their ages ranged from 3 weeks to 92 years. Most were admitted for elective surgery and could therefore be regarded as relatively good operative risks, but a considerable minority by reason of age, general condition, or specific pathology, required very careful management, and a few had such a precarious hold on life that the administration of any anaesthetic was fraught with danger. In some of the patients admitted for elective surgery studies of respiratory, cardiovascular and electro-encephalographic responses were undertaken, but it is not intended to give a detailed analysis of our own cases, but to refer only to observations which emphasize some of the pharmacological aspects of halothane.

Clinical experience has confirmed the claim by Raventós (1956) that halothane is capable of rapid, effective, and flexible anaesthesia. Because it is neither explosive nor inflammable it offers advantages in a wide field of anaesthetic practice. The potency of the drug makes low concentrations effective and also necessitates an accurate control of the vapour strength. The use of the drug without such accuracy of control is potentially dangerous and the interpretation of changes observed may be difficult. It is necessary, therefore, to give some consideration to the various methods of administration employed in the studies to be discussed.

TECHNIQUES OF ADMINISTRATION

In the first clinical trials (Johnstone, 1956), halothane was vaporized from a specially calibrated Trilene bottle by a high flow of gases and administered through a Magill attachment. This system was a fortunate choice for within limits it provided a relatively constant concentration under the direct control of the anaesthetist. Later, largely on account of expense, this technique was modified to reduce the consumption of halothane, and for this purpose a semiclosed technique using a Waters canister and a gas flow of 2–4 litres per minute was employed (Brennan, Hunter and Johnstone, 1957). In addition to reducing the consumption of halothane this to-and-fro method also might be expected to provide a constant concentration of vapour.

For a proper assessment of the changes during clinical anaesthesia in man there is no doubt that the most satisfactory method of administering halothane is by means of a nonrebreathing system incorporating a calibrated vaporizer (Falkner Hill, 1957; Brennan, 1957), whereby the concentration of vapour inhaled can be maintained at a constant level. This is not to deny that in the hands of an experienced anaesthetist the circle system can provide satisfactory clinical anaesthesia (Marrett, 1957), but it must be emphasized that no closed or semiclosed circle system with the vaporizer included in the circle can provide a constant concentration indefinitely under all conditions. Any alteration in the respiratory rate, in the tidal volume, or in the rate of leakage from the system will alter the concentration of halothane in the inspired mixture. In normal circumstances this is of little consequence, as when the patient is breathing spontaneously, the changes tend to be self-limiting (Marrett, 1959), and both Burton (1958) and Marrett have shown that when a concentration of 2.5 per cent or less is employed continuously for less than 90 minutes there is no accumulation of halothane within the circle during spontaneous respiration. This is presumably because the body tissues can absorb halothane from the blood faster than it is supplied through the lungs; but it is obvious that such absorption cannot continue indefinitely, and that the higher the concentration and the more prolonged the procedure the more readily will tissue saturation be reached. Ultimately then, dangerous concentrations of vapour may accumulate if the necessary adjustments in vapour strength are not made. The factors involved have been adequately discussed by Newman (1958). When controlled respiration is employed, this self-limiting safety mechanism is eliminated and it has been shown that, in these circumstances, halothane concentrations in the inspired gases may rise rapidly (Burton, 1958; Marrett, 1957). This is particularly true if the vaporizer setting is unaltered and the flow of fresh gases remains unchanged.

If the above interpretation is correct it follows that, under the conditions described, substitution of controlled respiration for spontaneous breathing is a dangerous manoeuvre and further that it is likely to be more dangerous towards the end of prolonged procedures than at the beginning, conclusions borne out by reference to the accounts of cardiac arrest under halothane described in the literature (Abajian et al., 1958; Chang et al., 1957; Foster, 1957; Hudon et al., 1957; Kirschner, 1957; Stephen et al., 1957). For this reason it is recommended that if controlled respiration is to be employed with any form of closed circle system the vaporizer should be excluded from the circle, and there is much to be said for Marrett's suggestion that if it can be avoided controlled respiration should not be used during halothane anaesthesia.

The methods of administration employed in our own series have followed the patterns just outlined. The first 150 patients were anaesthetized by the original method described by Johnstone (1956). Then a closed circle system with the vaporizer in the circuit was tried, but this method was soon abandoned because it was found to be impossible to maintain a constant concentration at all times during anaesthesia and a return was made to the use of the semiclosed nonrebreathing system with a calibrated vaporizer. Later, for the sake of economy, the semiclosed technique employing the Waters canister was introduced (Brennan et al., 1957), and this had the added advantage of being suitable for controlled respiration. Most anaesthetics in our series were given by one or other of these two methods, but experience was also gained with the Engstrom respirator and various forms of circle systems. In addition a few patients were anaesthetized by the open-drop method.

EFFECTS ON CENTRAL NERVOUS SYSTEM

The potency of halothane as an anaesthetic agent is now firmly established and most anaesthetists have been impressed by the ease and smoothness of induction whether by open-drop methods or in combination with nitrous oxide and oxygen. Once anaesthesia is begun the abolition of reflexes and the depression of vital activities resemble the pattern described for ether by Guedel (1936) although the time relationships are altered.

Unlike ether, induction of anaesthesia with halothane alone, in our experience, with which Robson and Sheridan (1957) are in agreement, is not usually associated with any degree of excite-

ment, but evidence to the contrary has also been published. Mackay (1957) reported a short stage of excitement in patients induced with halothane, while Stephen et al. (1957) described a brief but intense period of excitement in the majority of their patients similarly induced. It is, however, generally agreed that the stimulating properties of halothane are slight, and that induction is normally accompanied by the absence of tears and salivation. At the same time the suppression of pharyngeal and tracheobronchial secretions reduces the incidence of coughing.

Once induction is begun unconsciousness supervenes rapidly and the stage of surgical anaesthesia is usually reached within 5 minutes. Both pharyngeal and laryngeal reflexes are depressed quickly so that intubation can be undertaken early and is usually easy because the masseter muscles are relaxed. If for any reason the process of intubation is delayed, there is a prompt return of reflexes and further exposure to halothane vapour may be necessary before the manoeuvre can be completed.

The planes of surgical anaesthesia are most readily judged by the advancing paralysis of the intercostal muscles. Once intercostal paralysis is complete respiratory arrest may develop rapidly, particularly in young children, but if oxygenation is adequate normal breathing will return spontaneously, presumably because tissue absorption very quickly lowers the plasma concentration of halothane.

Attempts have been made to gauge the level of surgical anaesthesia by means of e.e.g. monitoring, and Given, Little and Tovell (1957) claim that there is good correlation between the appearance of the e.e.g. tracings and the depth of anaesthesia. This contention is supported by Robson and Sheridan (1957) who demonstrated characteristic e.e.g. changes and related them to blood concentrations of halothane. It should be noted, however, that in this latter series the e.e.g. changes could also be related to altered blood pressure levels. Gain and Paletz (1957), on the other hand, were unable to correlate the e.e.g. patterns with the clinical signs of anaesthesia, and Burnap, Galla and Vandam (1958) reported that the electroencephalograph was of little help in determining the depth of anaesthesia, as both adequate and inadequate surgical conditions were associated with a similar pattern. This work confirms our own impression, gained from a series of thirty patients monitored throughout anaesthesia, that there is no direct relationship between the e.e.g. and the level of anaesthesia, and that indeed the correlation between the e.e.g. pattern and the blood pressure level was more consistent. This observation requires further investigation, if it is to be substantiated, although again it is worth noting that electroencephalographic changes associated with hypotension have previously been described (Bromage, 1953).

Despite the early onset of surgical anaesthesia the specific analgesic properties of halothane are weak (Bryce-Smith and O'Brien, 1956), particularly when used as the sole anaesthetic agent (Löfström, 1958), and this weak analgesic action may explain the restlessness that has been widely described during recovery from halothane anaesthesia.

The autonomic response to halothane is of considerable importance and the general reduction of secretions is evidence of parasympathetic depression. The vagotonic action of halothane, on the other hand, is equally well recognized and many investigators have stressed the need for adequate premedication with atropine as protection against possible circulatory disturbances. Its depressant action on the sympathetic nervous system is also not in doubt, but there is lack of agreement on the means by which this effect is produced. The factors involved will be discussed in detail later in this paper, but one aspect of ganglion block ought to be mentioned at this stage; this is the potentiating effect of halothane on the ganglion blocking properties of tubocurarine. Severe hypotension may follow the intravenous injection of tubocurarine, and for this reason considerable care is required if these two drugs are to be used simultaneously.

Halothane also enhances the neuromuscular blocking action of tubocurarine (Burn et al., 1957; Watland et al., 1957), although there is no evidence that it possesses any specific action of its own at the motor endplate. Another explanation is therefore needed for the adequate muscle relaxation that occurs clinically and this has been attributed to the central effect of the drug (Watland, et al., 1957).

THE CIRCULATORY EFFECTS

The behaviour of the pulse rate during halothane anaesthesia varies considerably and no consistent pattern can be described. In his first series Johnstone (1956) reported that the pulse rate invariably became slower and rates as low as 40 beats per minute were observed by Bryce-Smith and O'Brien (1956) when the blood pressure fell during induction. Similar slow pulse rates were described in the medical Research Council Report (Burns et al., 1957). This bradycardia was regarded by Johnstone as evidence of vagal inhibition and in his later cases he preceded induction with an intravenous injection of 0.5 mg atropine. In this series bradycardia was less evident and an average of 84 beats per minute was reported (Johnstone, 1956). In this respect halothane resembles chloroform in that the bradycardia associated with the induction of anaesthesia can be abolished by intravenous atropine (Payne, 1955). The absence of reports of bradycardia in later papers suggests that premedication with atropine has been generally adopted. One other possibility, however, should be considered. In the initial period of the clinical trials with halothane, the concentration employed for induction and maintenance was generally higher than that commonly used later and it may be that bradycardia was a feature of the unnecessarily deep anaesthesia obtained (Robson and Sheridan, 1957).

As with many other anaesthetic agents halothane anaesthesia is sometimes associated with cardiac irregularities which vary greatly in their type and frequency. Absent or inverted P waves associated with the bradycardia just described emphasize the influence of vagal inhibition, and the restitution of normal sinus rhythm by intravenous atropine reinforces that view. Ventricular extrasystoles provide another group of arrhythmias; sometimes only occasional extrasystoles are noted, but more commonly bursts of unifocal ventricular extrasystoles coupled with sinus beats are seen. Rarely the multifocal variety has been described. These latter cases followed the subcutaneous injection of adrenaline and were reported by Brindle and his colleagues (Brindle et al., 1957; Millar et al., 1958), who concluded that the combination of halothane and adrenaline was potentially dangerous in man. Considerably more clinical experience will be required before this conclusion can be refuted, but it is worth noting that many groups (Bryce-Smith and O'Brien, 1956; Hudon et al., 1957; Marrett, 1957; Mackay, 1957) including ourselves have used the combination freely without incident.

On the whole disturbances in cardiac rhythm during halothane anaesthesia are not considered to be intrinsically dangerous (Brennan et al., 1957) but they may well draw attention to some irregularity in the administration of the drug as shown by the following example from our case records.

Case Record.

A healthy young woman was undergoing a radical mastoidectomy under general anaesthesia (nitrous oxide and oxygen 5:3 litres/min and halothane). Multifocal ventricular extrasystoles suddenly developed associated with a noticeable increase in the respiratory rate and tidal volume. Examination of the machine revealed that the carbon dioxide control had inadvertently been opened to give a 20 per cent concentration of carbon dioxide in the inhaled mixture. As soon as this was corrected the ventricular extrasystoles disappeared without any alteration in the halothane vaporizer setting.

In only one of our patients was it thought safer to abandon the use of halothane. This patient was a 20-year-old girl with a congenital heart anomaly consisting of transposition of the pulmonary veins, an atrioseptal defect and pulmonary stenosis, in whom extrasystoles appeared within 10 minutes of introducing halothane vapour. During the course of the anaesthetic these extrasystoles, which were multifocal in origin, became more frequent and ultimately completely dominated the monitoring screen. For this reason halothane administration was discontinued and almost immediately the multifocal extrasystoles disappeared.

A feature of halothane anaesthesia is the almost inevitable hypotension that accompanies induction. Originally observed by Johnstone (1956) it has been reported widely since and there is considerable evidence accumulating to indicate that the degree of hypotension obtained is directly related to the concentration of drug employed (Severinghaus and Cullen, 1958; Hudon et al., 1957; Stephen et al., 1957). This suggests that hypotension is a function of the depth of anaesthesia and ought to be reduced or indeed eliminated by careful administration. In our own series a slight degree of hypotension was observed in nearly every case. After the initial hypotension

following the inhalation of halothane there was a gradual recovery which tended to coincide with the application of surgical stimuli and which stabilized usually slightly below the conscious level (see also Dobkin, 1958). Further hypotension, except in a few cases to be described, was only seen when uncompensated bleeding occurred.

The mechanism by which hypotension occurs is not clear. Raventós (1956b), on the basis of experiments involving plethysmography of abdominal viscera and contractions of the nictitating membrane in the cat, concluded that it was due to a selective ganglion blocking action of the drug, the mesenteric ganglia being the most sensitive. Burn et al. (1957) disagreed with this conclusion not only because they were unable to demonstrate any strong ganglion blocking action when the nictitating membrane preparation was used, but also because they found that hypotension still occurred in cats that had been eviscerated. Further, they observed a fall in cardiac output in the dog's heart-lung preparation, and concluded that two additional factors ought to be considered; namely a distinct depressant action on heart muscle and a central depression of the vasomotor mechanism.

Evidence of myocardial depression during halothane anaesthesia in man has been presented by Severinghaus and Cullen (1958). These authors showed that during sympathetic blockade with both spinal anaesthesia and trimetaphan, artificial ventilation with 1.5 per cent halothane produced a greater reduction in cardiac output, arterial pressure, and stroke volume than when sympathetic blockade was not employed. They further showed that the fall in cardiac output was proportional to the degree of hypotension, and that it was associated with an increased peripheral resistance. From these results it was concluded that halothane has a direct depressant effect on the myocardium and no significant ganglion blocking action.

Further studies on the cardiovascular effects of halothane have been carried out in normal children by McGregor et al. (1958) and in adult volunteers by Wyant et al. (1958). Using the Evans blue dye dilution technique McGregor and his colleagues demonstrated a reduction in cardiac output during moderate and deep anaesthesia, but were reluctant to ascribe it to myocardial depression. Unlike Severinghaus and Cullen they were unable to show any significant change in peripheral resistance. Also using the dye dilution technique Wyant and his group carried out their investigations by means of serial cardiac outputs and concluded that the fall in peripheral resistance was the main cause of the hypotension observed, and that there was no serious impairment of cardiovascular efficiency until overdosage with halothane had been achieved. When this occurred there was a compensatory increase in peripheral resistance which tended to maintain the circulation despite the low output.

There seems little doubt that halothane in heavy dosage in common with other anaesthetics, does have a depressant effect on the heart, but in contrast to the findings of Severinghaus and Cullen, and McGregor et al., Payne, Gardiner and Verner (1959) have shown that when patients premedicated with atropine and allowed to breathe spontaneously are anaesthetized with halothane alone, the fall in blood pressure is often associated with increased cardiac output. This suggests that there is a lowered peripheral resistance partially compensated for by an increase in cardiac output. The rise in skin temperature and the increased finger volume observed in man during halothane anaesthesia (Payne, unpublished data) together with the experimental study of Hall and Norris (1958), which showed a net increase in pulse pressure, provide further evidence of peripheral vasodilatation. The extreme sensitivity of patients under halothane anaesthesia to sudden changes in posture also points to a depression of the vasomotor system (Burnap, Galla and Vandam, 1958). Finally, the fall in body temperature which has been reported by Löfström (1958) and which probably gives rise to the frequent occurrence of postanaesthetic shivering can be explained on the same basis.

It seems probable from the above data that when the atropinized patient is exposed to halothane concentrations of not more than 2 per cent the heart is able to compensate for a decrease in peripheral resistance, thus minimizing the blood pressure fall. In higher concentrations, especially when controlled respiration is used, this mechanism may fail, leading to profound hypotension and even cardiac arrest.

Clinically the relationship between high concen-

trations of halothane, controlled respiration, and circulatory failure has been repeatedly observed since Foster reported the first death during halothane anaesthesia in 1957. Reports of cardiac arrest continue to be published and it is remarkable how consistent these are. Typically, immediately before a sudden severe fall in blood pressure the anaesthetist has begun controlled respiration on a circle system with the vaporizer included in the circle. From what has been said previously a rapid increase in vapour concentration can be postulated and this together with the known deleterious effect of positive pressure respiration on the haemodynamics (Cathcart et al., 1958) may very well explain the sudden catastrophe.

In our own series four patients developed profound hypotension. In two of these anaesthesia was maintained by a closed circle system using a Marrett machine. A sudden, severe fall in blood pressure occurred when controlled respiration was started after the intravenous injection of 40 mg of suxamethonium to facilitate cholangiography. In both cases the exclusion of halothane from the circuit and ventilation with pure oxygen followed by the return of spontaneous breathing restored the blood pressure to normal levels. We have since abandoned the use of controlled respiration at any time when halothane is vaporized in a closed circle system.

In the remaining two patients chlorpromazine had been given pre-operatively; in one instance the drug was given for 6 weeks previously but was withdrawn 5 days before operation; in the other patient chlorpromazine was used as premedication. In both cases the blood pressure fell alarmingly soon after anaesthesia was established and proved to be extremely difficult to control throughout the course of the administration. In a number of other patients, premedication with chlorpromazine or an allied compound was associated with a labile blood pressure which, while not giving cause for anxiety, nevertheless emphasized the need for care when such drugs are used. On theoretical grounds Brennan, Hunter and Johnstone (1957) suggested that the use of chlorpromazine and other adrenolytic drugs was contra-indicated during halothane anaesthesia. It is our view that insufficient attention has been paid to the risks involved when these drugs are used together, especially if combined with controlled respiration. Unfortunately, in all cases where circulatory difficulties were encountered during halothane anaesthesia, the premedication has not always been described, but there is sufficient evidence in the literature (Mackay, 1957) to warrant a more detailed assessment of the combined effects of these two drugs.

RESPIRATORY EFFECTS

The effects of halothane on respiration are complex. The vapour is nonirritant and relatively high concentrations are tolerated during induction even in highly premedicated patients. These advantages have been particularly appreciated by those workers engaged in the investigation of the respiratory effects of halothane as the absence of coughing and straining has greatly facilitated their clinical measurements.

Although Raventós (1956) showed that in dogs exposed to halothane the respiratory rate was decreased, an observation confirmed by Hall and Norris (1958), it is now well established that in man the respiratory rate is increased during halothane anaesthesia and a frequency of 50 breaths per minute has been reported (Chang et al., 1957). An outstanding feature of our own experience with the drug was the almost immediate return to normal rates when halothane was withdrawn. This observation suggested that the tachypnoea may be due to an irritant effect of the vapour on the stretch receptors of the lung but attempts to substantiate this hypothesis have so far proved unsuccessful.

Synchronous with the increased rate there is a reduction in the tidal air with the result that the minute volume is either unchanged or even slightly decreased during surgical anaesthesia. It is obvious, therefore, that the alveolar ventilation must be reduced. When tachypnoea becomes excessive the tidal air is lowered still further and the alveolar ventilation becomes inadequate, with a rise in arterial carbon dioxide tension (Holmdahl and Payne, 1959). Because of the high oxygen concentrations commonly used in the inhaled mixtures, such inadequacy is usually masked in anaesthetic practice, but Bryce-Smith and O'Brien (1956) effectively verified this assumption by

demonstrating the development of cyanosis in a group of patients breathing a halothane-air mixture.

The degree of carbon dioxide retention due to insufficient ventilation has been studied by end-tidal air analysis (Devine et al., 1958; Long and Pittinger, 1958) and by the measurement of the carbon dioxide tension of arterial blood (Holmdahl and Payne, 1959). In the latter investigation the rise in arterial carbon dioxide tension was less than that expected from the observed decrease in alveolar ventilation, and it was concluded that the production of carbon dioxide must be depressed during halothane anaesthesia. Although the possibility of an altered production of carbon dioxide was mentioned by Devine et al. (1958) it was not specifically investigated by them; but it seems likely from their data that such a depression did occur if it is assumed that the end-tidal air samples were truly alveolar and that a steady state of anaesthesia had been established when the measurements were made.

METABOLIC EFFECTS

The diminished carbon dioxide production described above might have been anticipated from the work of Severinghaus and Cullen (1958) who showed that the oxygen uptake fell in proportion to the increase in concentration of halothane breathed in a group of six patients. They postulated that this fall was due to the muscle relaxation and to the reduced respiratory and cardiac work associated with exposure to the drug. In one of their patients who showed a marked depression of cardiac output, stroke volume, blood pressure and oxygen consumption, and whose mixed venous blood oxygen saturation fell from 79 per cent to 51 per cent, it was observed that, despite the severe cardiovascular depression and increased oxygen utilization, there was no evidence of shock nor of metabolic acidosis. The absence of metabolic acidosis during halothane anaesthesia was confirmed by Holmdahl and Payne (1959), who in addition to studying the effects of the drug on ventilation also investigated the acid-base state of their patients.

Other metabolic aspects of halothane that have been investigated are those concerned with the activity of the liver and the kidney. Raventós (1956) carried out hepatic and renal function tests in rats and dogs exposed to repeated anaesthesia with halothane and found no significant changes in the results before and after exposure; but histological examination of the liver and kidneys in animals sacrificed when the experiments were completed showed unspecified minor changes in the liver, and in the kidney dilatation of the proximal convoluted tubules associated with slight cytological changes in the cells of those tubules. Chronic toxicity tests were repeated by Krantz et al. (1958), but they were unable to find evidence of histological damage either in the kidney, liver or brain of rats exposed to halothane.

In man blood sugar determinations made in twenty patients by Stephen et al. (1957), in an attempt to assess the effects of halothane on the liver were within normal limits. Burnap et al. (1958), however claimed that halothane raised the blood sugar level by interfering with the glucose phosphorylating mechanisms, but pointed out that in this respect its effect was no greater than cyclopropane or ether. This comparison between halothane and cyclopropane and ether was extended by Little and Barbour (1958) who applied a series of five liver function tests without demonstrating any difference in response.

Evidence of definitely abnormal results in liver function tests after prolonged anaesthesia with halothane has been provided by Brindle et al. (1957), but they were careful to state that the disturbance observed was probably no greater than that produced by other agents in the same circumstances. A similar conclusion was reached by Burns et al. (1957), who reported that despite a high incidence of deterioration in both liver and kidney function tests, after halothane there was no substantial difference between the control group and the halothane series.

Although one death has been reported that could possibly be attributed to delayed halothane poisoning (Virtue and Payne, 1958) other factors were also involved and the general failure to demonstrate a standard pattern of hepatic damage suggests that the drug has no specific toxic action on the liver and that any damage that does occur results from the combination of halothane anaesthesia with such potentially dangerous hazards as hypoxia, prolonged hypotension and pre-existing liver disease.

EFFECTS ON THE UTERUS

In the early experimental studies carried out to assess the value of halothane its effects on the uterus were comparatively neglected. The first clinical report of its use in obstetric practice suggested that halothane would find a place in most obstetric units as a substitute for chloroform, but the authors reported that of 233 patients studied 27 mothers had a period of reduced uterine tone following halothane anaesthesia and a further 4 had postpartum haemorrhages (Robson and Sheridan, 1957). These findings are in agreement with those of Russell (1958) who observed that after Caesarean section the uterus occasionally failed to contract in patients given halothane, and Dixon and Matheson (1958) who described the occurrence of retained placenta and postpartum haemorrhage after halothane.

The inhibition of contractility by halothane in the human pregnant uterus was demonstrated by Embrey, Garrett and Pryer (1958). By means of tocographic recordings these investigators showed that halothane depressed both spontaneous contractility and contractions artificially induced with intravenous oxytocin. Embrey and his colleagues were impressed by the rapidity with which the inhibitory effect developed on exposure to halothane and by the speed with which activity returned when consciousness was restored, and they pointed out, notwithstanding the potential dangers of uterine relaxation in certain circumstances, this property of halothane might be of considerable value in the management of such conditions as constriction ring and threatened uterine rupture.

CONCLUSION

Since halothane was first introduced in 1956 it has been the subject of a large number of clinical and experimental studies. Indeed it is unlikely that any other new drug has had so much attention in so short a time from chemists, physiologists, pharmacologists and clinicians with the result that not only has a great deal been learned about halothane but its introduction has also provoked the re-assessment of other anaesthetic drugs.

On the whole the claim by Raventós that halothane is capable of rapid, effective and flexible anaesthesia has been substantiated. Because it is neither explosive nor inflammable, it is of particular value in a wide field of surgery and its tendency to produce hypotension can be utilized to advantage in many specialties, especially as some understanding of the hypotensive mechanism has now been reached.

The safety of halothane has been virtually proved by its use in many hundreds of thousands of anaesthetics without incident and, though several cases of cardiac arrest have been reported, the recognition that the use of controlled respiration combined with a closed circle system incorporating a halothane vaporizer can lead to dangerously high concentrations of inspired vapour ought to eliminate this hazard in the future.

The nonirritant nature of halothane vapour produces a peaceful induction with quiet breathing once anaesthesia is established. There is some evidence that carbon dioxide may accumulate but this has not proved troublesome in practice and the absence of any marked metabolic disturbance emphasizes its safety.

The ability of halothane to inhibit the contractility of the human pregnant uterus explains the occasional occurrence of retained placenta and postpartum haemorrhage and defines its limitations in obstetric practice.

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SERNYL (C1-395) IN CLINICAL ANAESTHESIA

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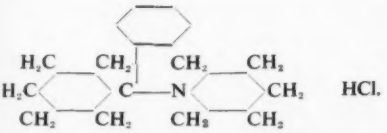
SERNYL is an analgesic agent recently synthetized in the Detroit laboratories of Parke, Davis and Company. It is a white solid, freely soluble in water and ethanol: I-(I-phenylcyclohexyl) piperidine, monohydrochloride.



Comprehensive investigation of its effects in several animal species revealed potent analgesic activity without evidence of cellular toxicity. The intravenous administration of 0.3–0.6 mg/kg to monkeys induced a cataleptoid state which lasted up to 1 hour during which time major surgery could be performed without difficulty whilst the animals appeared to be awake and alert. The oral administration of somewhat larger doses to cats and dogs produced similar results. Doses in excess of those required for "surgical anaesthesia" tended to cause excitation and convulsions in these animals. These studies, which included tests in healthy volunteers, will be reported elsewhere.

The first clinical trial was performed by Greifenstein et al. (1958). They observed that the drug, in doses of 0.25 mg/kg of body weight, produced complete analgesia which permitted the performance of operations such as skin-grafting, orthopaedic procedures, even gastrectomy and cholecystectomy although the muscular relaxation in the latter was not considered to be adequate. Within a few minutes after the intravenous injection of the drug the patients appeared to lose consciousness and became unresponsive to painful and auditory stimuli. Doses in the region of 1 mg/kg tended to cause excitation unrelated to the surgical procedure; this reaction was adequately controlled by the intravenous administration of either pentobarbital or thiamylal sodium.

Greifenstein and his associates observed that Seryn1 increased the respiratory minute volume in all patients. Systolic and diastolic blood pressures were consistently elevated by the drug, and pulse rates were increased in some patients and slightly decreased in others. Electrocardiography revealed no evidence of arrhythmia. Moderate changes were observed in the electroencephalographic patterns unlike those associated with natural or barbiturate-induced sleep. Reflex activity was unimpaired by moderate doses. Vertical nystagmus appeared in all patients and sometimes persisted for 24 to 36 hours postoperatively, associated with diplopia and vertigo.

When the drug was made available to us, along with the pharmacological and initial clinical reports, it was decided to investigate its use in the three phases of surgical treatment: pre-operative sedation, surgical anaesthesia and postoperative analgesia. Preliminary tests confirmed all the observations of Greifenstein and his associates and indicated that an initial dose of 10 mg, either intravenously or intramuscularly, could be used safely and conveniently for all adult patients. Children were not included in the early stages of the trial.

PRE-OPERATIVE SEDATION

Forty-two patients have been investigated, their ages ranging from 20 years to 73 years. The operations consisted of herniorrhaphy, haemorrhoidectomy, gastrectomy, cholecystectomy, mas-

tectomy, thyroidectomy, and prostatectomy. Each patient received Sernyl 10 mg intramuscularly 1 hour before the operation. As the mental reactions of the patients to the drug seemed to be related more closely to their ages than to any other factor, they have been grouped according to age, 60 years of age being arbitrarily selected as the dividing line. Twelve of the patients were over 60 years and thirty were between 20 years and 60 years of age. The results were as follows:

Patients over 60 years.

On arrival at the operating theatre nine of them were asleep but rousable, disorientated, and completely oblivious of their surroundings. Two were happily euphoric but well orientated and amused by the fact that they were about to be operated upon. One patient was emotionally unaffected by the drug and complained of dizziness and diplopia.

Patients under 60 years.

Nine patients (eight females) on arrival at the operating theatre were euphoric and stated that they felt happy and unworried. Three were asleep but rousable with difficulty and completely disorientated. Four patients (one male and three females) were excited, talkative, and not fully co-operative—two of them incessantly recited poetry and two sang in a drunken manner. Hallucinations occurred in four patients within 30 minutes after the administration of the drug and two of them became restless and agitated: one thought he had become a grub and another was convinced he had been shot into space in a sputnik; the third was under the impression he had died and ascended into heaven; the fourth believed herself to be listening to the Hallé Orchestra in the Free Trade Hall in Manchester. In seven patients (five young males and two females) the drug had no obvious effect, each of them being fully conscious and apprehensive.

Three patients for emergency operation, who were in severe pain, very apprehensive and agitated, were each given 10 mg of Sernyl intravenously shortly before the operations were due to start. One, a thin frightened female of 34 years, had acute vertebral osteomyelitis with nerve root pressure, the second was a robust agitated male of 34 years with a perforated gastric ulcer; and the third was a muscular young labourer with a comminuted fracture of his tibia and fibula. The injection of Sernyl was immediately followed by maniacal excitement in the peritonitis and osteomyelitis cases, and the fracture case became noisy and abusive though his pain seemed to disappear completely. The excitement in these cases was satisfactorily controlled by thiopentone injected intravenously.

There was no evidence of respiratory depression in any of these patients after the administration of Sernyl and blood pressure remained either unaltered or elevated, the average increase in systolic pressure being 23 mm Hg. Pulse rates remained within normal limits. On arrival at the operating theatre anaesthesia was induced in each patient with thiopentone-atropine and maintained with halothane-oxygen, using suxamethonium for additional relaxation as required. Sernyl premedication caused no obvious changes in the reactions of the patients to thiopentone, atropine, halothane, or suxamethonium. Atropine was still required to prevent vagal inhibition of the heart when halothane was administered. The sensitivity of the peripheral circulation to the pressor action of methoxamine was uninfluenced by Sernyl. On recovery from anaesthesia twenty-nine patients had no recollection of their journey to the operating theatre.

POSTOPERATIVE ANALGESIA

Sernyl 10 mg was administered intramuscularly to each of 50 patients at the conclusion of major operations performed under halothane-oxygen anaesthesia. The operations included laparotomies, major orthopaedic procedures, laminectomy, herniorrhaphy, mastectomy, thyroidectomy, thoracotomy, haemorrhoidectomy, nephrectomy, nephrolithotomy, prostatectomy and colporrhaphy.

Complete postoperative analgesia, lasting from 4 to 6 hours, was provided for skin, subcutaneous tissue, muscle, bone, joints, pelvic floor, and perineum. Pain was sometimes experienced after operations involving the peritoneum, kidney and ureter, testis, and coeliac plexus. The drug was particularly effective in relieving the pain of orthopaedic operations, colporrhaphy, haemorrhoidectomy, mastectomy, thyroidectomy, and prostatectomy. It did not significantly delay the recovery of consciousness and caused no cardiovascular or respiratory depression. The patients remained fully co-operative and excitement and

delirium were seldom observed in those patients who had been under inhalational anaesthesia for at least 30 minutes before the injection of Sernyl. Most patients remained lightly asleep for 2 to 3 hours postoperatively but could be easily roused during this period and were somewhat disorientated and unaware that the operations had been performed. The incidence of transient postoperative vomiting was unchanged (4 per cent) and occurred only after upper abdominal operations.

SURGICAL ANAESTHESIA

Sixty-seven patients have been anaesthetized with Sernyl as a sole agent. Their ages ranged from 18 years to 90 years. The operations included cystoscopy with diathermy, biopsy, or ureteric catheterization (23 cases); uterine dilatation with curettage or hysterosalpingography (14 cases); amputation of the lower limb (8 cases); ligature of varicose veins (8 cases); haemorrhoidectomy (6 cases); orthopaedic operations (5 cases); secondary wound suture and skin grafting (3 cases). Each patient was premedicated with pethidine 50 mg and atropine 0.6 mg, and arrived at the operating theatre fully conscious.

Sernyl (10 to 20 mg) was administered intravenously to each patient. Within a few minutes each patient lapsed into either a catatonic stupor or a state of akinetic mutism and ceased to react to painful stimuli as tested by pin-prick and squeezing the Achilles tendon. The limbs became moderately relaxed and the tendon reflexes remained brisk, the abdominal skin reflexes were unchanged and the plantar reflexes were flexor. The eyes often remained widely open, staring fixedly into infinity with the conjunctival and pupillary reflexes either unimpaired or sluggish. The pharyngeal and laryngeal reflexes remained normal and full muscle tone persisted in these structures with the result that the air passages remained unobstructed and jaw support and artificial airways were not required. Attempts to insert artificial airways or laryngoscopes were usually resisted by clenching of the jaws, coughing, salivation, and spitting.

With the 10-mg doses of Sernyl the patients could usually respond weakly to instructions and several of them appeared to be in ecstatic trances, repeatedly whispering such words as "heavenly", "beautiful", or "lovely"; two of them believed they were in the presence of God. With the 20-mg doses most of the patients, particularly the females, were completely unresponsive for periods up to 1½ hours. There was no evidence of respiratory depression in any of the patients.

Muscular relaxation though not complete was usually adequate for the operations performed. Laparotomies were avoided mainly because Sernyl failed to provide complete analgesia of the peritoneum and coeliac area, and for other reasons which will be referred to later.

The duration of the catatonic stupor was closely related to the age and sex of the patient. With the older patients it usually lasted for 1 to 2 hours and gradually disappeared with the return of normal consciousness. In the young and middle-aged groups, particularly the males, the stupor was often followed in 15 to 20 minutes by a noisy and restless delirium which in three cases progressed to maniacal excitement necessitating forceful restraint by several of the nursing staff for up to 3 hours postoperatively.

Tachycardia and hypertension were commonly observed (78 per cent of cases) within a few minutes after the intravenous injection of Sernyl 10 to 20 mg and invariably occurred before the operation started. In a few cases, mainly young male adults, this complication was of an alarming severity and was immediately terminated by the intravenous administration of thiopentone 250 mg followed by halothane-oxygen. Tachycardia and hypertension did not occur when Sernyl was administered intravenously to patients already rendered lightly asleep by narcotics such as thiopentone, nitrous oxide, or halothane and we are therefore of the opinion that the cardiovascular reaction is related to the hallucinosis rather than to direct stimulation of the cardiovascular system or its vasomotor control. An electrocardiographic investigation of ten patients has shown that the tachycardia is of sinus origin and isolated ventricular extrasystoles are sometimes observed in patients with established essential hypertension. Sernyl 10 mg has been administered intravenously to eleven patients with essential hypertension—three with electrocardiographic evidence of hypertensive heart disease—and no deleterious effects have been observed apart from slight increases in the pulse rates and in the already raised blood

pressures. In all cases, the cardiovascular effects of Sernyl subsided in about 40 minutes.

SERNYL ANAESTHESIA WITH SUPPLEMENTARY NARCOSIS

Sernyl 20 mg intravenously failed to provide adequate anaesthesia in seventeen patients, all young or middle-aged adults. Attempts to secure better operating conditions by the injection of further 5-mg doses did not produce results as predictable as they should be in the circumstances so it was considered safer to supplement with conventional anaesthetic agents. Nitrous oxide was the first supplementary agent to be used and caused severe clonic convulsions in the first two cases after 2 to 3 minutes inhalation of an 80 per cent mixture with oxygen; the convulsions were immediately abolished by thiopentone 250 mg intravenously. Thiopentone was subsequently used as the agent of choice for the induction of anaesthesia in patients already under the influence of Sernyl and no further trouble has been encountered. The indications for supplementary anaesthesia were as follows:

Noisy delirium with rambling and incoherent speech.
Inadequate muscular relaxation.
Purposeless movements, including head rolling and arm waving.
Persistent priapism during herniorrhaphy.
Tachycardia and hypertension.

EMERGENCE FROM SERNYL ANAESTHESIA

Behaviour during the emergence from Sernyl anaesthesia again appears to be dictated by the age and sex of the patient. Old people remain quiet and free from pain—excluding some upper abdominal laparotomies—for several hours postoperatively and are often unaware that they have been to the operating theatre and have had operations performed on them. Euphoria is common and they frequently state that they feel many years younger.

Young and middle-aged patients are often noisy and excited for several hours afterwards and describe vestibular and proprioceptive hallucinations with distortion of vision. Females are usually in a happily drunken state and do not require any special supervision other than that normally provided by the recovery ward staff. Males, on the other hand, can be violent and aggressive to a degree which requires constant supervision for up to 3 hours—these reactions are most often observed after the 20-mg doses of Sernyl.

Complete amnesia lasting for 3 to 4 hours after the injection is usual in the older people but the younger patient, although having no recollection of the operation or the return to the ward, sometimes on recovery will describe unpleasant hallucinations. Postoperative analgesia is complete and several patients, particularly those subjected to endoscopies and other nontraumatic procedures, have complained of a feeling of generalized numbness lasting for 24 hours postoperatively.

SERNYL ANAESTHESIA AND CONVENTIONAL ANAESTHESIA SUBJECTIVELY COMPARED

Ten patients have been investigated, all of whom were undergoing review cystoscopy for papilloma of the bladder. Each patient had had several previous anaesthesias with either thiopentone-nitrous oxide or thiopentone-halothane. Their ages ranged from 18 years to 73 years. Premedication was with pethidine 50 mg and atropine 0.6 mg. On arrival at the operating theatre Sernyl 10 to 20 mg was injected intravenously and the endoscopy started. The results were as follows:

Four elderly patients, each of whom was over 65 years of age, were satisfactorily anaesthetized with 10 mg of Sernyl. There was complete amnesia for the operation and for 2 hours afterwards. Emergence was smooth and without restlessness.

Two females of 34 years and 46 years had cystoscopy performed without difficulty after Sernyl 10 mg in each case. Shortly after their return to the ward both patients talked and sang incessantly for over 2 hours. On questioning the following day neither had any recollection of the operation, but both were conscious of the fact that they had behaved in a silly manner during emergence and were embarrassed by the recollection.

Four robust males were initially anaesthetized with Sernyl 20 mg each, injected intravenously. Supplementary thiopentone-halothane was required in each case after about 15 minutes because of noisy delirium or violent and purposeless movements. Each of these patients was restless and excited for several hours afterwards and on

the following day was very critical of the method of anaesthesia which had been used, stating that it was the most unpleasant ever experienced. None of them had any recollection of the operation and their complaints were directed against the hallucinations experienced during emergence, in addition to a feeling of generalized numbness which lasted for almost 24 hours after the operation. One of them, a lorry-driver by occupation, complained of muscular inco-ordination and distortion of vision which persisted for several days. Each of these patients requested that this type of anaesthesia should not be used at any subsequent examination he might require.

ILLUSTRATIVE CASE HISTORIES

CASE 1.

Female, 51 years of age; heart and lungs normal; blood pressure 150/80 mm Hg. For excision of the head of the right radius fractured by a fall 24 hours previously. Premedicated with pethidine 50 mg and atropine 0.6 mg. Patient fully conscious on arrival at the operating theatre and unable to rotate the right forearm because of pain in the fracture site; very tender on pressing the upper end of the right radius. Sernyl 10 mg was injected intravenously and the patient immediately went into an akinetic trance and, after 3 minutes, did not react to vigorous rotation of the injured forearm or to pressure on the fracture site. The blood pressure rose to 190/90 mm Hg and the pulse rate increased from 85 to 110 beats a minute. A tourniquet was applied and the operation started.

The patient did not react in any way to the incision of the skin, muscles, periostium, ligaments, joint, and bone structures. Twenty minutes after the injection of Sernyl she opened her eyes and, for the remainder of the operation, conversed intelligently and normally with the theatre staff; by this time her blood pressure and pulse rate had returned to normal levels. Throughout the operation no pain or discomfort of any kind was felt and no visual abnormalities were experienced, nor was there any alteration in her emotional state and she remained completely orientated. She had no difficulty in performing any movement requested, including movements of the right forearm.

No pain or discomfort was experienced for 24 hours after the operation and no sedation was required. Her memory of the operation was completely intact, including the time and manner of applying the tourniquet, at which time she appeared to be in a state of akinetic mutism.

CASE 2.

Female, 90 years, with senile dementia. Acute intestinal obstruction of several days duration; gross abdominal distension. Agitated and violently resistant to examination and attempts at resuscitation. Sernyl 10 mg slowly injected intravenously and the patient became quiet and co-operative in 15 minutes. She then tolerated without protest the passage of a Ryle's stomach tube and the setting up of an intravenous saline transfusion. No changes occurred in the blood pressure and pulse rate which remained at 140/100 mm Hg, and 125 beats a minute respectively. Restlessness recurred 4 hours later. The patient died on the following day.

CASE 3.

Male, 73 years. Active and ambulant. Admitted to the outpatient department with acute retention of urine due to a urethral stricture. Had eaten a large meal 2 hours previously. Sernyl 10 mg administered intravenously. The usual akinetic trance ensued and the patient was placed in the lithotomy position without difficulty and the bouginage started. He was apparently asleep and unrousable for 20 minutes. He then wakened suddenly and was highly euphoric but fully co-operative. He stated that he felt 50 years younger, just as though he had been "born again". The difficult and traumatic bouginage lasted 40 minutes, during which time the patient felt no pain or discomfort. He was delighted with the experience and remained free from pain for 24 hours.

CASE 4.

Obese male, 59 years. Completely disrupted nephrectomy wound 7 days after operation. Considered unfit for conventional anaesthesia because of acute or chronic bronchitis. No premedication. Sernyl 10 mg injected intravenously. The patient remained awake but became completely unaware of his whereabouts. There was no reaction to the insertion of deep and superficial sutures and he talked incoherently throughout the operation which lasted 35 minutes. One hour later he was fully conscious and orientated and remained analgesic for the next 8 hours. There was complete amnesia for the operation and for several hours he was completely unaware that he had been resutured.

CASE 5.

Male, 78 years. Ischaemic gangrene of the left leg. Mentally confused and disorientated. Febrile. Hypertensive heart disease with auricular fibrillation, ventricular rate 130 beats a minute. Blood pressure 210/120 mm Hg. Signs of incipient bronchopneumonia. For mid-thigh amputation of left leg. No premedication. Sernyl 10 mg injected intravenously. Patient's mental state remained unaltered and in 5 minutes he ceased to respond to pinprick and squeezing of the Achilles tendon. The amputation was then performed without difficulty and the patient returned to the ward. The following day he was rational and unaware that an operation had been performed. Recovery was uneventful.

CASE 6.

Female, 40 years. For excision of a large and chronically indurated fissure-in-ano. No premedication. Heart and lungs normal, blood pressure 150/90 mm Hg, pulse rate 85 beats a minute. Sernyl 20 mg injected intravenously. The patient immediately lapsed into the usual trance and responded feebly to questioning. The blood pressure rose to 170/100 mm Hg and the pulse rate increased to 115 beats a minute. Throughout the operation the patient appeared to be lightly asleep and could easily be awakened to answer questions in a rather incoherent voice. The operation was completed without difficulty in 20 minutes. During this time she felt no pain or discomfort and could not be convinced that she was actually undergoing surgical treatment.

She remained free from pain for 12 hours afterwards but was rather noisy, talkative, and disorientated. Her husband, who visited her on the evening of the day of operation, complained to the ward sister that his wife seemed "queer" and did not recognize him. The following day the patient was perfectly normal and orientated and had no memory of the previous day's events.

CASE 7.

Male, 30 years. Orchidectomy for seminoma. Heart and lungs normal, blood pressure 120/70 mm Hg. Premedicated with pethidine 50 mg and atropine 0.6 mg. Fully conscious and apprehensive on arrival at the operating theatre. Sernyl 20 mg injected intravenously caused sleep in 2 minutes and the patient could not be roused. The pulse rate remained unchanged at 70 beats a minute and the blood pressure rose to 140/80 mm Hg. Incision of the skin and subcutaneous tissue of the inguinal region caused priapism without any reaction in the limbs. When the testis was handled he suddenly opened his eyes and made rather violent movements of his arms and legs. Thiopentone 250 mg was injected intravenously and anaesthesia was continued uneventfully with halothane-oxygen. There was no postoperative pain or restlessness and amnesia was complete for the operation and for 18 hours afterwards.

CASE 8.

Robust male, 30 years. For open reduction and bone graft to a simple fracture of the tibia and fibula. Heart and lungs normal, blood pressure 120/70 mm Hg. Premedicated with pethidine 50 mg and atropine 0.6 mg. Fully conscious and unworried on arrival at the operating theatre, pulse rate 70 beats a minute. Sernyl 20 mg injected intravenously. The patient immediately went into a trance with his eyes widely open and staring fixedly and fearfully into infinity. The blood pressure rapidly increased to 210/120 mm Hg and the pulse rate rose to 175 beats a minute. Respirations became rapid and deep at 55 a minute and were accompanied by a low moaning. Thiopentone 250 mg was injected intravenously and anaesthesia continued with halothane-oxygen; within 5 minutes the pulse rate had dropped to 80 beats a minute and the blood pressure had returned to 120/70 mm Hg. The operation was successfully completed in 50 minutes and the patient returned to the ward in good condition. No pain was felt for 12 hours afterwards but during this time he tended to be rather noisy and occasionally swore violently in a loud voice; there was no restlessness. The following day the patient was perfectly rational and had complete amnesia from the time of the initial injection of Sernyl till 12 hours later.

CASE 9.

Robust male, 57 years. Cystoscopy. Premedicated with pethidine 50 mg and atropine 0.6 mg. Sernyl 20 mg intravenously induced sleep from which the patient could not be roused. He was then placed in the lithotomy position without difficulty and the cystoscope passed without any reaction. Ten minutes later, whilst the cystoscopic examination was progressing quietly, the patient suddenly made violent movements of his arms and legs but remained unconscious. Thiopentone 250 mg was injected intravenously and anaesthesia smoothly maintained with halothane-oxygen. The examination was completed 7 minutes later and the patient returned to the ward. For the next 3 hours he struggled violently and appeared to be in a state of acute maniacal excitement which gradually subsided without specific therapy. The following day the patient described unpleasant recollections of an hallucination in which he believed he had been buried alive and had struggled violently to escape. He was rather angry about the method of anaesthesia as he had previous experience of several conventional anaesthesias which did not cause any postoperative disturbances.

CONCLUSIONS

Sernyl is undoubtedly the most potent general analgesic agent which has yet been used in clinical medicine. It is highly effective for pain arising in skin, subcutaneous tissue, muscle, bone, joints, pelvic floor, and perineum. It does not appear, in the doses used in this trial, to give complete relief from pain arising in the peritoneum, coeliac plexus, kidney, and testis. It has the unique advantage over other sedatives and analgesics that it does not cause depression of cardiovascular and respiratory functions and can be safely used in elderly patients when opiates and other agents are contra-indicated. Another outstanding advantage is that doses sufficient to permit such painful operations as haemorrhoidectomy or skin-grafting fail to cause any depression of pharyngeal and laryngeal reflexes, thereby eliminating the risk of respiratory obstruction from anatomical causes; jaw support and artificial airways are quite unnecessary during Sernyl anaesthesia and analgesia.

The usefulness of the drug is limited by the excitation which it sometimes causes and which may persist for 12 hours after a single dose. The excitation has a disturbing resemblance to the acute toxic psychoses and is often associated with delirium and hallucinations which, although usually of a highly pleasurable nature, are sometimes rather terrifying to the patient. The psychotic reaction is encountered most frequently in young or middle-aged males and the most violent forms followed the 20-mg doses of Sernyl. On recovery from the effects of the drug the patient may be able to recall the rough outline of the hallucination, which, when of the unpleasant variety, can be embarrassing to all concerned. The milder degrees of excitation, which resemble the effects of alcohol, although harmless and often amusing, can be a source of worry to other patients and visitors.

Sernyl excitation has not been encountered in elderly patients, the mental reaction to the drug in this group being essentially an akinetic euphoria. Agitated states have not been observed in patients who have been given Sernyl after at least 30 minutes of inhalational anaesthesia with halothane-oxygen. It can therefore be concluded that Sernyl is a safe and effective analgesic agent in the following circumstances:

(1) As a sole anaesthetic agent for elderly hospitalized patients undergoing relatively superficial operations and endoscopies when anaesthesia with conventional agents is considered inadvisable. It has also provided satisfactory operating conditions in younger patients but the psychological reactions in these groups are too unpredictable to permit its routine use as a sole agent for surgical anaesthesia.

(2) Sernyl in 10-mg doses postoperatively provides excellent relief from pain arising in skin, muscle, bone, joints, perineum, and pelvic floor. Excitement is suppressed by the previous administration of halothane-oxygen.

(3) Sernyl is a useful supplement to conventional anaesthesia in operations involving the perineum and pelvic floor. The respiratory and cardiovascular reactions associated with surgical stimulation of these parts during light anaesthesia are eliminated by Sernyl 10 mg preferably administered intravenously after the induction of anaesthesia with thiopentone-halothane.

ACKNOWLEDGMENT

We are indebted to Parke Davis and Company, Detroit, Michigan, for generous supplies of Sernyl (C1-395), and to Mr. J. B. Lloyd, Manchester Royal Infirmary, and Mr. W. Phillips, Crumpsall Hospital, for dispensing the drug in ampoule form.

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Brit. J. Anaesth. (1959), **31**, 440.

METHOD FOR THE ESTIMATION OF OXYGEN IN GAS MIXTURES CONTAINING NITROUS OXIDE

BY

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STANDARD methods for the estimation of oxygen concentration cannot be used when the gaseous mixture contains components which are very soluble in water. This is because the measurement of the fractional change in volume or pressure which occurs on the removal of oxygen is complicated by the solubility of the water-soluble components in the absorbing reagent. The problem has been especially trying for anaesthetists because of their frequent use of nitrous oxide-oxygen mixtures. We have attempted to overcome the difficulty by making use of the reaction employed by Exton, Schattner, Korman and Rose (1945) in their method for the estimation of the oxygen content of whole blood.

In principle, our method requires the precise measurement of a small volume of gas at a known temperature and pressure. The sample is then introduced into an aqueous suspension of ferrous hydroxide. The latter reacts quantitatively with oxygen to form a ferric compound, nitrous oxide being chemically inert in these circumstances. Sulphosalicylic acid is then added, which combines with the ferric iron to produce a coloured complex whose concentration can be estimated by spectrophotometry. The quantity of oxygen is expressed in terms of mass, and this can be converted to volume at the appropriate temperature and pressure. A feature of the method is that it can be adapted to determine oxygen concentration over a very wide range.

DESCRIPTION OF APPARATUS AND TECHNIQUE OF ANALYSIS

The apparatus, illustrated in figure 1, consists essentially of a small gas burette contained in a water-jacket. The burette has two bulbs and is made from 1-mm Pyrex capillary tubing. These bulbs are intended to contain approximately 0.15 ml and 0.4 ml respectively and the volume of gas analyzed is dependent upon the oxygen concentration in the mixture. Calibration is effected by the repeated analysis of air or oxygen. Introduction of the sample is achieved by manipulation of a mercury reservoir and taps and this measured volume of gas is ejected into a syringe containing ferrous hydroxide reagent. Tap A3 is a two-way tap with an L-shaped plug. In "open position 1", the burette is connected to the sample inlet. In "open position 2", the reservoir R2 is connected to the sample inlet. To perform an analysis, taps A1 and A2 are opened and A3 is turned to "open position 1". The reservoir R1 is raised to fill the burette, taps and side-tube with mercury. Tap A1 is closed. The vessel containing the gas sample is attached to the Inlet I. In our apparatus this consists of a perspex adaptor designed to hold a Record syringe. Tap A1 is opened and the reservoir R1 is lowered to draw in slightly more than the desired volume of sample. Taps A1 and A3 are closed, the sample is allowed to attain temperature equilibrium and the screw-clip C is adjusted so that the mercury meniscus stands exactly at the chosen mark in the burette. Tap A2 is now closed. The gas sample is at slight supra-atmospheric pressure so tap A3 is opened briefly to allow the gas to reduce to atmospheric pressure. Tap A3 is then rotated to "open position 2" and the tap-bore and side-tube are filled with mercury. This tap is now closed. A syringe containing air-free ferrous hydroxide reagent is applied to the adaptor. Taps A1, A2, and A3 are opened (in this order) and the whole of the gas sample, together with a little mercury, is displaced under positive pressure into the reaction syringe. All taps are closed. The gas is entrapped in the syringe which is then cautiously removed. A little mercury is displaced from it and a mercury-filled,

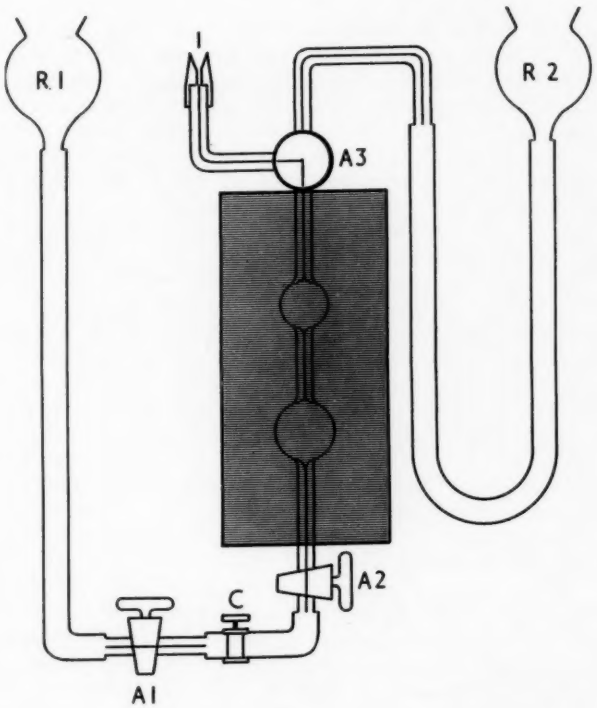

FIG. 1

sealed-off needle-hub applied to exclude air. The syringe is shaken mechanically in a transverse plane for 15 minutes. At the end of this time, 2 ml of sulphosalycylic acid reagent are drawn into the syringe and this immediately terminates the reaction. After this stage the solution can be safely exposed to the air. The colour complex develops to its maximum in 1 minute and the contents of the syringe are transferred into a measuring cylinder with three washings of water, each of 5 ml. The solution is diluted to a known volume, the optical density of the colour is determined in a convenient colorimeter and this is compared with a standard solution of ammonium ferric sulphate. We have employed both the Unicam SP600 and the EEL portable colorimeter, using a wavelength of 500 mμ or the yellow-green filter No. 626. With the EEL it is advisable to adjust the dilution of both standard and unknown solutions so that the optical densities fall within the same narrow range on the galvanometer. In this way some of the advantages of a null method are secured. Calibration curves prepared on the Unicam SP600 and the EEL colorimeter are shown in figure 2. The optical density of the ferric sulphosalicylate complex solution varies in accordance with Beer's law. In this instance the calibration curves were prepared by serial dilution of a stock standard of ammonium ferric sulphate, adding 2 ml of sulphosalicylic acid reagent and adjusting the volume to 10 ml. One thousand micrograms of iron are equivalent to 144 μg of oxygen, the mass of 100 μl of the gas at S.T.P.

Although the description of the method is lengthy the method in practice is straightforward and rapid, and it is particularly suitable for serial analysis. Measurement of the gas sample requires 2 minutes. If reagent syringes and a suitable

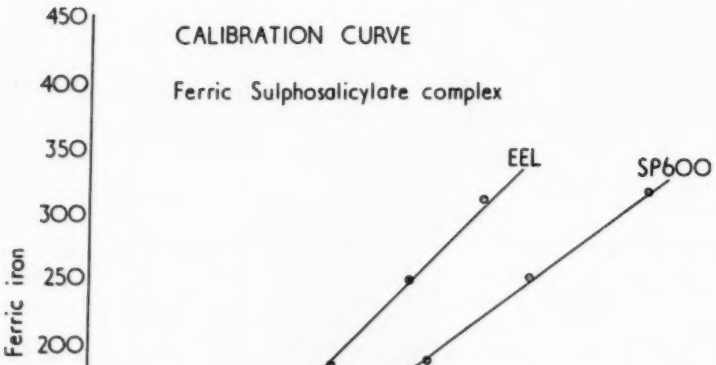

FIG. 2

shaker are available, several samples can be dealt with simultaneously at this stage. The introduction of sulphosalicylic acid, dilution and estimation of optical density needs about 2 minutes for each sample.

PREPARATION OF REAGENTS

The reagent solutions necessarily contain small amounts of dissolved oxygen. It is therefore essential to determine a reagent blank with each batch of analyses. Nevertheless, for maximum sensitivity of the method it is desirable that the optical density of the blank should be as low as possible, and this can be achieved by preparing the ferrous hydroxide, free from air, in the following manner.

A solution of borax, 2 per cent w/v, is made from Analar grade hydrated sodium tetraborate. To this solution is added 0.5 per cent v/v Lissapol. The purpose of this "wetting agent" is to ensure that the gas in the syringe will disperse freely. This has been shown to increase the rate of solution of the oxygen in the reagent very materially. We have tried various methods of removing oxygen from the borax solution. Boiling under reflux and reduced pressure with subsequent storage under liquid paraffin was found to be unsatisfactory. We now bubble a stream of nitrogen through the borax solution. The nitrogen is freed from any residual oxygen by passing it first through alkaline pyrogallol solution.

A solution of ferrous sulphate, 10 per cent w/v is prepared from the Analar grade hydrated salt. The solution is boiled gently for 1 minute to facilitate the removal of oxygen in solution as insoluble ferric hydroxide. The loss of ferrous iron by this procedure is unimportant. The oxygen-free ferrous sulphate is transferred to a centrifuge tube, covered with liquid paraffin and centrifuged to remove insoluble material. The reagent is best prepared fresh each day.

To prepare the ferrous hydroxide reagent approximately 5 ml of oxygen-free borax solution are sucked into a 10-ml all-glass syringe containing a glass bead. The solution is introduced through a long fine-bore needle. Gentle suction on the syringe is usually sufficient to prevent air bubbles forming, but any minute bubbles are quickly displaced by rotation of the glass bead and ejected. This solution is rejected and the procedure is repeated leaving approximately 1 ml of borax solution in the syringe. One millilitre of ferrous sulphate is next introduced directly from the centrifuge tube, avoiding disturbance of the packed precipitate. This is followed by a further 4 ml of borax solution. These volumes are not critical and may be measured by the graduations on the syringe. The needle is left in place and the contents are mixed by rotation. The syringe is now ready for use as previously described.

Sulphosalicylic acid reagent 25 per cent w/v is prepared from Analar grade hydrated acid. It need not be airfree.

A standard solution of ferric iron, used for the calibration curve and as a reference solution, is prepared from Analar ammonium ferric sulphate. A convenient stock standard solution contains 300 μg of ferric iron per millilitre and to it is added 4 ml of sulphosalicylic acid reagent in each 100 ml. The acid is used to prevent decomposition of the iron alum solution. The solution is stable at room temperature and it appears to remain so for long periods. Appropriate dilutions are made prior to use.

DISCUSSION

In any method which depends upon the precise measurement of a gas volume, it is necessary to examine how accurately this may be done. Two burettes, A and B, have been used. Repeated analyses of air and oxygen for the calibration of each burette gave the results tabulated in table I. The consistency of these can be seen. Although the apparatus has been designed so that only gases and no liquids enter the burette, the presence of a soluble gas might conceivably interfere with this consistency if contamination of the burette with water occurred during use. To test the validity of this point, two mixtures containing nitrous oxide and oxygen were prepared and repeated analyses made from the same sample. The results are shown in table II. No serial error is apparent, there being no significant difference between the mean of the first and the last three estimations. Table III shows the results of analyses of various mixtures of oxygen, nitrous oxide and of commercial grade carbon dioxide. All these mixtures were made by passing the gases through a water-sealed gas meter and collecting them in 40-litre polythene bags.

The properties of the reaction whereby the colour complex is produced must also be examined. Ferrous hydroxide can be obtained as a white precipitate when a solution of a ferrous salt in oxygen-free water is treated with an alkali, but the precipitate is white only in the complete absence of oxygen. It very readily absorbs oxygen, becoming first a dirty green, then black and finally reddish brown in colour. The reaction requires suitable conditions of hydrogen ion concentration. A concentration of borax between 1 per cent and 3 per cent satisfies these conditions, a 2 per cent solution having a hydrogen ion concentration equivalent to pH 9.2.

Between pH 5.8 and pH 12.2, and in the presence of molar concentrations of each reagent, excess of oxygen leads to the formation of magnetite (Fe_3O_4). However, under our experimental conditions it is necessary to have an excess of ferrous iron, and this results in incomplete oxidation and the probable formation of ferrous-ferrite ($Fe(FeO_2)_2$). We did not determine the nature of this compound as it reacted quantitatively with sulphosalicylic acid.

Sulphosalicylic acid is well known as a reagent for the estimation of ferric iron although some doubt exists as to the exact nature of the complex formed. The colour of this complex can be varied with change of pH. Foley and Anderson (1948) studied this problem and concluded that in solutions acid to pH 2.4, only one complex is formed and its stability is a function of the acidity of the solution due to change in the degree of ionization of the sulphonic acid grouping. We have observed no significant variation in the optical density of this acid complex when the concentration of sulphosalicylic acid is varied between 3 per cent and 30 per cent.

The formation of the ferric sulphosalicylate is complete within 1 minute and the colour remains stable for 24 hours. It is not affected by ordinary

TABLE I

Calibration of gas burettes

No. of determinations	Gas burette	Estimated mass of O_2 in sample in micrograms	Calculated volume of bulb at 20°C and 760 mm Hg (ml)
6	A O_2, 1st mark	209·3 (210·0–209·0) S.D. 0·43	0·156
6	A Air, 2nd mark	147·0 (149·0–145·3) S.D. 1·30	0·525
20	B O_2, 1st mark	204·7 (206·3–201·8) S.D. 1·18	0·152
10	B Air, 2nd mark	150·8 (152·2–150·0) S.D. 0·94	0·540

TABLE II

Repeated analysis of O_2/N_2O mixtures. Reproducibility of method.

No. of determinations	Volume of gas (ml)	Estimated mass of O_2 in sample in micrograms	% oxygen found in sample	% oxygen predicted
24	0·525	40·6 (39·5–41·5) S.D. 0·65	5·75 (5·60–5·87) S.D. 0·09	5·55
6	0·525	89·0 (88·0–90·0) S.D. 1·44	12·60 (12·46–12·75) S.D. 0·24	12·50

TABLE III

Analysis of gas mixtures.

Mixture	Volume of gas (ml)	Estimated mass of O_2 in sample in micrograms	% oxygen found in sample	% oxygen predicted
N_2O	0·525	0·01	0·002	——
CO_2	0·525	3·2	0·45	——
O_2/N_2O	0·156	103·8	49·4	50·0
,,	0·156	105·2	50·1	50·0
,,	0·156	105·2	50·1	50·0
,,	0·525	175·5	24·8	25·0
,,	0·156	190·0	90·5	90·0
,,	0·156	200·0	95·5	95·0

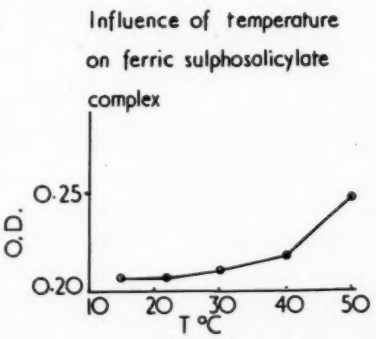

FIG. 3

daylight but is thermosensitive (fig. 3), the change being reversible below 50°C. It is apparent from figure 3 that the variation introduced in the normal range of room temperature is insignificant. If it was desirable to perform the analysis at a temperature above 22°C, a calibration curve would have to be prepared at the appropriate temperature.

SUMMARY

(1) A method is described for the estimation of oxygen in gas mixtures containing nitrous oxide.

(2) The method appears to be specific for oxygen and it will detect less than 0.1 μg of oxygen.

(3) The method can easily be adapted to estimate oxygen over a wide range of concentration, and it requires 0.5 ml or less of gas for analysis.

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FACULTY OF ANAESTHETISTS
of the
ROYAL COLLEGE OF SURGEONS OF ENGLAND

The next Postgraduate Course in Anaesthetics will take place between February 8 and 19, 1960.

The Joseph Clover Lecture will be delivered by Dr. Lee at the Annual Meeting of the Faculty on Wednesday, March 16, 1960.

Brit. J. Anaesth. (1959), **31**, 446

THREE NONREBREATHING VALVES FOR USE IN ANAESTHESIA

BY

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THESE valves are designed to prevent rebreathing during spontaneous or intermittent positive pressure respiration. The transition from spontaneous to assisted or controlled ventilation is effected by sharply compressing the reservoir bag. The expiratory port is then automatically occluded, and the gases are directed into the patient. Expiration is initiated by releasing the pressure on the bag. The inspiratory port is immediately closed and the expired gases pass to the atmosphere (fig. 1).

The general principle is common to several rebreathing valves of this type (Sykes, 1959) but most suffer to a certain extent from two defects. Firstly, movement of the valve flaps may be sluggish. This results in leakage of gas past the valve during the initial part of each phase. A rapid rise and fall in the applied pressure curve will help minimize this defect. Secondly, there is a tendency for the valve to stick in the inspiratory position when controlled respiration is being employed or when the gas inflow exceeds the minute volume. This tendency is accentuated by the presence of moisture on the expiratory valve seating. An attempt has therefore been made to overcome these difficulties by employing large valve flaps inclined at an angle to the gas streams, so that a powerful turning movement is achieved. In this way the valves are moved in both directions by the flow of gas, and the spring loading is merely employed to maintain the valve in the expiratory position against gravity. The spring also ensures that the reservoir bag fills adequately during expiration and the expiratory pause (Mushin and Mapleson, 1954).

Mark I.

In this, the earliest model, the valve flaps consist of perspex discs cemented on to an axle and set at an angle of 75 degrees to each other, a principle similar to that used by Neff and Lind (1945). The axle pivots in the wall of the valve box and the valve seatings are arranged so that there is a clearance of $\frac{5}{16}$ of an inch at the free edge of the open valves. The driving flap (over the inflow port) is twice the area of the horizontal disc and a light spring assists return to the expiratory position at rest. The expiratory port is knife-edged to reduce sticking when wet. Various forms of expiratory valves were used on this and subsequent models but a thin rubber flap valve has been found to be perfectly satisfactory. This is set at an angle to the expiratory tube so that it is of oval shape. It is attached by cement at its narrow end (Kaye, 1949) and protected by a collar.

Mark II and III.

The two valve flaps are replaced by one which is pivoted to swing between the contiguous ends of the inflow and outflow tubes. The relation of these tubes determines whether the valve is of the right-angle or straight-through type. In either event a very light spring retains the flap in the expiratory position at rest. Again, the angle which the flap makes with the expiratory stream of gas and the size of the flap are determining factors in the efficiency of the valve.

The Mark III valve (figs. 2 and 3) is basically similar to the Lewis modification of the Leigh valve (Lewis, 1956). However, it has been found unnecessary to provide a safety blow-off within the valve. The expired gas impinges directly on the edges of the valve flap which is thus returned immediately to the expiratory position. The inlet tube in both valves is tapered to fit an expiratory valve mount and the tube leading to the patient takes either a facepiece, angle piece or a catheter mount.

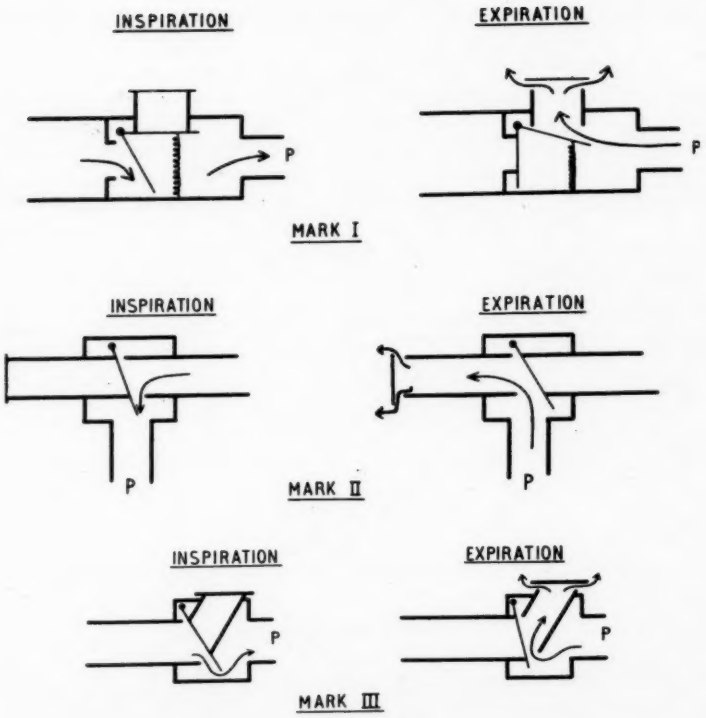

FIG. 1
Three nonrebreathing valves for use in anaesthesia. P=patient.

FIG. 2
Mark III valve. The matchstick is inserted through the inflow port and wedges the valve flap in the mid-position.

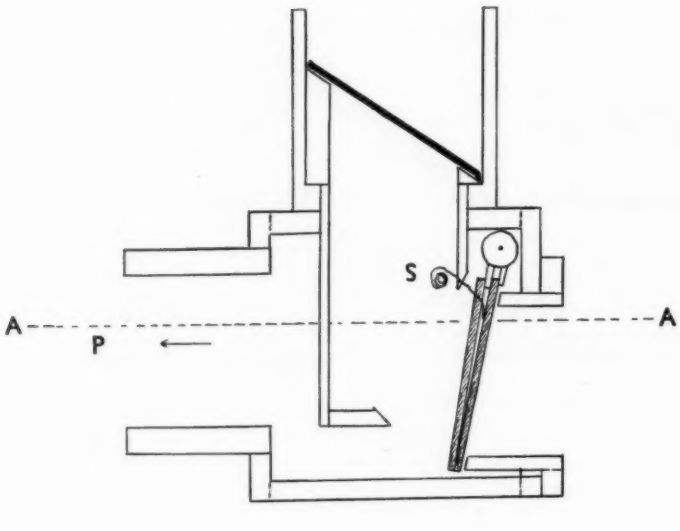

FIG. 3
Diagrams to show constructional details of Mark III valve.
Top: Longitudinal section. Bottom: Horizontal section across A—A.
P=Patient. S=Spring.

TABLE I
Resistance of three nonrebreathing valves to continuous airflow.
Expiratory flow resistances were recorded both with and without the rubber flap expiratory valve so as to reveal the influence of altered design.

Flow rate (air l./min)	*Inspiration* (cm H_2O)			*Expiration* (flap present) (cm H_2O)			*Expiration* (flap removed) (cm H_2O)		
	Mk I	Mk II	Mk III	Mk I	Mk II	Mk III	Mk I	Mk II	Mk III
15	0·2	0·2	0·3	0·2	0·4	0·4	0·0	0·1	0·1
20	0·3	0·3	0·4	0·3	0·6	0·5	0·1	0·1	0·1
30	0·4	0·3	0·4	0·3	0·8	0·6	0·1	0·2	0·2
40	0·5	0·4	0·4	0·4	1·1	0·8	0·1	0·4	0·3
50	0·6	0·5	0·4	0·5	1·3	1·1	0·2	0·5	0·4
60	1·0	0·7	0·5	0·6	1·5	1·5	0·2	0·6	0·5

In use these valves can be interposed between the expiratory valve mount and the patient either on the Magill attachment (Mapleson "A") or more conveniently on the Mapleson "C" system (Mapleson, 1954). When using the latter arrangement a "walk-around" extension may be inserted between the reservoir bag and valve mount. This increases the mobility of the anaesthetist and acts as a silencer for the valve. With both systems the Heidbrink-type expiratory valve may be used to prevent over-distension of the reservoir bag.

The resistances of the valves are shown in table I.

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FACULTY OF ANAESTHETISTS
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Burroughs Wellcome Fellowships

The Burroughs Wellcome Fund in the U.S.A. has founded a Fellowship in Anaesthesia at the University of California Medical Center, Los Angeles, to give a British physician in training in anaesthetics the opportunity of the cultural, academic and professional experience of an American University and to increase the understanding of anaesthetics between the physicians of the United States and Great Britain. The value of the Fellowship is 4,000 dollars per annum, including travelling expenses. This amount has been found by the first Fellow to be adequate to cover normal requirements. The Fellowship has been founded for three years to support three Fellows for one year each, and the Fellows are expected to return to Britain upon the completion of the terms of their respective Fellowships. The Fellowship is for both clinical and research work.

Anaesthetists who have passed at least the Primary Examination for the F.F.A.R.C.S. are invited to apply for the third annual award. The Fellow appointed will be expected to take up his duties as soon as possible after September 1, 1960. Applications, giving details of qualifications and experience (including research experience, if any) and the names of two persons to whom reference may be made if necessary, should be sent to R. S. Johnson-Gilbert, Esq., M.A., Secretary, Faculty of Anaesthetists, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2., not later than Monday, February 8, 1960.

R. S. JOHNSON-GILBERT,
Secretary,
Faculty of Anaesthetists

Brit. J. Anaesth. (1959), **31**, 450

REVIEW ARTICLE

NONREBREATHING VALVES

BY

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"MANY patients with difficulty acquire the habit of inhaling air from a bag and returning the air from their lungs through the nose . . . a mouthpiece has therefore been constructed with two valves of silk. . . . With this mouthpiece a person may breathe perfectly in their natural manner without straining the muscles of the chest and without any other subjection than the holding of a small pipe in their mouth. . . . " (Beddoes and Watt, 1796).

It is possible to show by means of a rapid gas analyzer that the end-expired gas is rapidly removed from the region of the mouth during normal respiration (fig. 1). The extent of rebreathing is therefore dependent on the volume of the deadspace and on the shape of the wave fronts within the deadspace. If an anaesthetic apparatus is connected to the respiratory tract it forms an extension to the deadspace already present in the patient. By suitable design this additional deadspace may be minimized. In fact, if endotracheal intubation is performed (thus bypassing the mouth, nose and pharynx) the total deadspace may be reduced below the normal for that individual.

Apparatus deadspace may be minimized most effectively by separating inspiratory and expiratory gas streams as close to the patient as possible. The valve system exercising directional control should also be close to the patient. If situated at some distance, as in most circle absorption systems, expired gas may diffuse into the inspiratory tube and be rebreathed. Mixing at this point may be accentuated by the use of intermittent positive pressure respiration.

The gas from the expiratory limb of such a valve system must then be passed either through an efficient carbon dioxide absorber, or to the atmosphere. In the latter case a supply of fresh gas equal to the patient's minute volume is required. If gas is in short supply or expensive this constitutes one disadvantage of the nonrebreathing system. There are possible disadvantages. One, for example, is the loss of moisture from the lungs, with a consequent increased tendency to the crusting of secretions. Against these must be set the following advantages:

(1) The hazards of carbon dioxide absorption (heat retention, inhalation of irritant dust, exhausted soda lime) are eliminated, and the necessity for bulky, complicated and expensive apparatus is abolished.

(2) The composition of the inspired gas is displayed on the flowmeters—there is no dilution with nitrogen, water vapour or carbon dioxide (Ruben, 1953). The dangers inherent in low gas flows (Crowley et al., 1948) are abolished.

(3) Denitrogenation and saturation with nitrous oxide are achieved with maximum speed, thus minimizing the dose of supplementary drugs required.

(4) The patient's minute volume can be estimated by adjusting the gas inflow until the reservoir bag is kept about three-quarters inflated at the end of expiration. The sum of the gas flows recorded on the flowmeters then equals the minute volume.

To function efficiently a nonrebreathing valve system should have negligible resistance at normal respiratory flow rates, a low intrinsic deadspace and minimal reflux. It should also be silent in action, and the valves should not stick when wet. The complete unit should be light, compact, and easily cleaned and serviced. Unless the valves are mechanically or electrically operated these requirements are difficult to satisfy, for the energy required to activate the valves must be expended by the patient or the anaesthetist, and must therefore constitute a resistance.

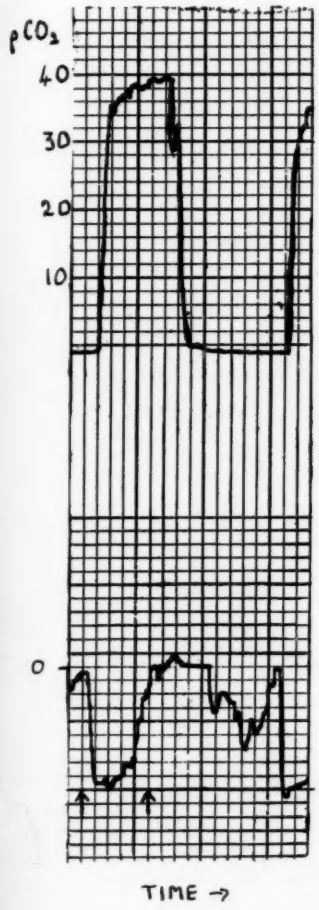

FIG. 1

Mass spectrometer tracings demonstrating the rapid drop in concentration of carbon dioxide in the mouth region during the expiratory pause. Quiet respiration through the open mouth.

Top tracing: P_{CO_2}. Tip of sampling catheter situated between the lips.

Bottom tracing: Argon flowmeter. The two arrows delineate the period of air flow during expiration.

Time: each vertical line =0.2 second.

Careful design can, however, minimize most of these defects (Kaye, 1949; Hunt, 1955).

Nonrebreathing valves can be classified into three categories—those suitable only for spontaneous respiration, those designed primarily for use with respirators and intermittent positive pressure respiration, and those which may be used during anaesthesia with either spontaneous or controlled respiration. Some observations on these valves are detailed in table I and their working principles are shown diagramatically in figures 2 and 3.

NONREBREATHING VALVES DESIGNED FOR USE WITH SPONTANEOUS RESPIRATION

The first valve of this type to be utilized for anaesthesia was that used by Morton on his first inhaler. " . . . The inspired air passes through the bottle but the expiration is directed by a valve in the mouthpiece, and escaping into the apartment is thus prevented from vitiating the medicated vapour" (Bigelow, 1847).

The original flap valves were made of leather but later other materials and other shapes of valve were used, such as the glass discs in Bell's ether inhaler of 1847 (Duncum 1947a) and the ball valves in Charriere's inhaler for ether (Duncum, 1947b). With the advent of the anaesthetic machine the nonrebreathing valve fell into disuse and interest was only revived by the description of a nonrebreathing valve incorporated in the expiratory valve mount of the Oxford ether vaporizer (Epstein, Macintosh and Mendelssohn, 1941). Leigh was the first to popularize the use of such a valve on the American continent when he described its use in paediatric anaesthesia (Leigh and Kester, 1948). This valve underwent many subsequent modifications (Stephen and Slater, 1948; Slater and Stephen, 1951), but the basic design has remained the same—a valve to prevent rebreathing, and an expiratory valve which prevents dilution of the inspired gas with room air. Such valves are now used extensively in paediatric anaesthesia in the United States and Canada. A simplified valve has been described (Smith, 1954) which works on the same principle and can be constructed easily by the anaesthetist. Another valve of this type which may be constructed from American surplus gasmask valves has been described by Cutter, Crepps and King

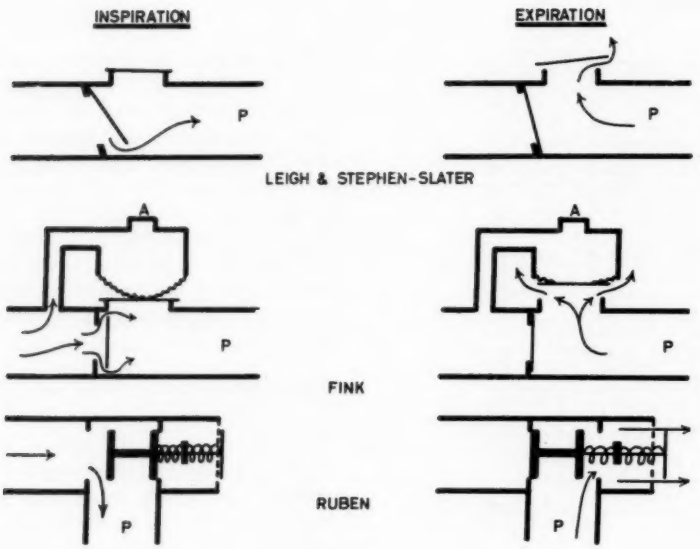

FIG. 2

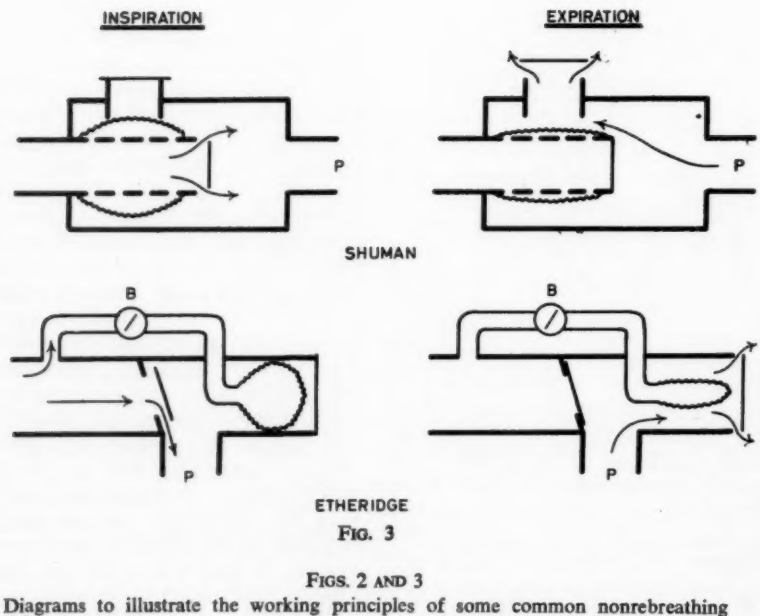

FIG. 3

FIGS. 2 AND 3

Diagrams to illustrate the working principles of some common nonrebreathing valves

P refers to the patient end of the valve.

A (Fink) marks the vent which is opened during spontaneous respiration to ensure that the pressure within the chamber remains at atmospheric.

B (Etheridge) is a three-way tap which occludes the bypass tube and vents the balloon to atmosphere during spontaneous respiration.

TABLE I

Resistance of some common nonrebreathing valves.

Measurements made using a continuous flow of air from a calibrated flowmeter. For comparison, figures are given for a tightly packed Waters canister with and without soda lime. The mean figures for three Heidbrink type expiratory valves taken at random from Magill attachments in routine use are also included.

Valve	Resistance to inspiratory flow (cm H_2O)						Resistance to expiratory flow (cm H_2O)					
	15	20	30	40	50	60 1/min	15	20	30	40	50	60 1/min
Stephen-Slater	0·9	1·1	1·7	2·1	2·5	2·8	0·6	0·8	1·3	2·0	2·6	3·5
Fink	0·9	1·3	1·9	2·5	3·1	4·0	0·4	0·5	0·8	1·3	1·8	2·1
Ruben	0·7	0·8	1·1	1·4	1·8	2·0	0·4	0·5	0·8	1·5	2·4	3·5
Shuman	1·0	1·3	1·7	2·0	2·8	4·0	0·6	0·8	1·2	1·5	1·8	2·4
Etheridge			0·5	0·8	1·2	1·4			0·8	1·0	1·2	1·3
Sykes Mk III	0·3	0·4	0·4	0·4	0·4	0·5	0·4	0·5	0·6	0·8	1·1	1·5
Waters canister (no pan scrubber)							0·2	0·4	0·6	0·8	1·2	1·5
Waters canister (plus pan scrubber)							0·3	0·4	0·7	1·0	1·4	1·8
Heidbrink type valves							2·5	2·7	3·2	3·5	4·0	4·6

(1954). Kirchoff and Burns (1953) have described a Y-shaped valve which has a deadspace of 12.5 ml and having satisfactory opening pressure and resistance.

Nonrebreathing valves have not been employed commonly for paediatric anaesthesia in this country because of the widespread use of the T-piece technique both with spontaneous respiration (Ayre, 1937, 1956) and controlled respiration (Rees, 1950). The T-piece technique has the advantage that resistance to air flow can be less than that of any pressure operated valve. On the other hand a gas flow approaching twice the patient's minute volume is necessary to prevent rebreathing (Inkster, 1956).

VALVES DESIGNED FOR USE WITH MECHANICAL RESPIRATORS

The use of these valves originated as a direct result of the Copenhagen poliomyelitis epidemic of 1952. Nonrebreathing valves were introduced to obviate the long-term use of soda lime and machines were developed to provide intermittent positive pressure respiration. The Stott valve (Smith, Spalding and Russell, 1954) which was fitted to the earlier Radcliffe respirators and the valve described by Galpine and Smith-Clarke (1955) are probably the best known examples of this type. Both work satisfactorily provided they are cleaned and dried regularly. In the newer respirators these pressure-operated valves have been superseded by electrically or mechanically operated valves which are more efficient and dependable (Smith-Clarke and Galpine, 1955; Russell et al., 1956).

The Cardiff inflating valve (Mushin, 1953) may also be mentioned here, although it was designed for use with the Oxford inflating bellows. Neff and Lind (1945) have also described an inflating valve which could be used with the Oxford inflating bellows. Since all these valves will admit

air if the patient breathes spontaneously they are not very suitable for use during anaesthesia.

NONREBREATHING VALVES SUITABLE FOR SPONTANEOUS AND CONTROLLED RESPIRATION

These valves are basically similar to the first group of valves mentioned in that they consist of an expiratory valve which allows gas to escape to the atmosphere and yet prevents the ingress of air during spontaneous respiration, and a nonreturn valve which prevents the return of gas to the anaesthetic machine or respirator. They differ in the methods employed to occlude the expiratory port during the positive pressure phase. This can be accomplished manually. For example, the Stephen-Slater valve can be used for intermittent positive pressure ventilation by occluding the expiratory port with the thumb while the bag is squeezed with the other hand. Ryan (1955) has designed a valve working on the same principle with a pushbutton over the expiratory valve. Whilst having the advantage of precise control this method does necessitate the use of both hands, and attempts have therefore been made to overcome this difficulty by utilizing the applied inspiratory pressure to close the expiratory port.

In 1954 Rattenborg described such a valve for the manual ventilation of polio patients. Though it could be applied to anaesthesia it was a little cumbersome. Fink (1954) described a simpler valve designed specifically for use in anaesthesia. A bypass from the bag side of the valve transmits pressure to a membrane on the outside of the expiratory valve. Thus the expiratory port is automatically occluded during inspiration. By turning a small knob on the top of the valve, the pressure chamber may be opened to the atmosphere and the valve then functions similarly to those mentioned in the first group. This valve has a deadspace of 11.5 ml and a suitably low resistance, and works excellently if properly maintained. A valve working on a similar principle has been described by Etheridge (1958). A bypass inflates a balloon which occludes the expiration tube. To prevent distension of the balloon during spontaneous respiration, when an excessive gas inflow might cause a pressure build-up on the inspiratory side, a tap is provided which occludes the bypass and vents the balloon to atmosphere. A rather more direct application of pressure to the expiratory valve is achieved by utilizing the principle of the Wilms's self-inflating cuff (Shuman, 1956). Such a valve is cheap, simple to make and silent in action, and has worked excellently in the author's hands (fig. 4).

Another principle employed is movement of a piston or synchronous movement of two disc valves which shuttle to and fro. The valve described by Newton et al. (1955) is an example of the piston type, and the Ruben (Ruben, 1954, 1955) employs a moving bobbin-shaped valve. The Ruben valve has undergone several years of intensive development and apart from the clicking noise which disturbs some surgeons, works excellently. Like all pressure-operated valves it will stick if the pressure is allowed to build up continuously within the system, but this can be avoided by incorporating a safety valve in the circuit or in the valve itself. If a Waters expiratory valve mount and bag is used to supply gas, the expiratory valve may be used to release excess pressure. A walk-around extension can be inserted between bag and mount if desired. This also has the effect of silencing the valve action. Further silencing can be achieved by a short length of corrugated tubing connected to the expiratory limb.

Other designs for this type of valve have been described by Lewis (1956) and the author (Sykes, 1959). In the latest of these a single flap swings between the exit and entry ports, the action being controlled by the angle which the flap makes with the direction of gas flow. Sticking can then be

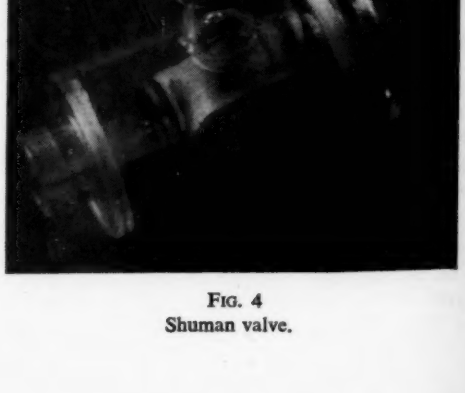

FIG. 4
Shuman valve.

caused only by the rapid application of firm and continuous pressure to the rebreathing bag—a feat only accomplished intentionally during anaesthesia. Recently Frumin et al. (1959) have described a modification of the Fink valve. This has the added advantage that if, during spontaneous respiration, the gas supply becomes inadequate, air is automatically admitted to the circuit through the expiratory port.

STERILIZATION

Valves made of perspex or similar plastic material cannot be sterilized by heat. However, the commercial hypochlorite antiseptic solutions (e.g. Milton) are effective when the valve is immersed in them for 20 minutes. The valve should afterwards be well washed under a tap and allowed to dry.

CONCLUSION

In the last few years a number of simple and effective nonrebreathing valves have been developed. Unfortunately, few of these valves are available commercially, but several valves have been described which can be constructed easily by the average hospital workshop and which will give years of reliable service. An increased demand for nonrebreathing valves would probably stimulate commercial production.

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MUSCLE WEAKNESS FOLLOWING THYROIDECTOMY

BY

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ACCORDING to Brain (1940) a variety of muscle disorders may be associated with disordered function of the thyroid gland. These are all characterized by a reduction in muscle tone.

The following case is considered worthy of reporting because of the severity of the muscle weakness which followed thyroidectomy for thyrotoxicosis, and because at one stage it was considered that the anaesthetic technique might have been the cause of the paresis.

CASE REPORT

A male, aged 27 years, had been seen 12 months previously when he complained of palpitations, loss of weight, sweating and nervousness. Investigations were carried out and a diagnosis of thyrotoxicosis was made. He was given the antithyroid drug carbimazole (Neomercazole) and this controlled his symptoms satisfactorily.

24.8.58. Carbimazole was discontinued and replaced by Lugol's iodine, 0.6 ml three times daily.

30.8.58. He was admitted to hospital for thyroidectomy.

2.9.58. Examination revealed a very obese young man weighing 111.4 kg (17.5 st). There were no symptoms of thyrotoxicosis but he had slight exophthalmos of his right eye. No tremor of his hands or evidence of nervousness was detected. The thyroid gland showed a moderate diffuse enlargement but swallowing was normal and the voice was unaffected. His haemoglobin was 15.8 g/100 ml (107 per cent Haldane), B.P. 145/90 mm Hg, pulse rate 72/minute. Urinary examination revealed no abnormality.

3.9.58. Thyroidectomy was performed under general anaesthesia the technique for which was as follows.

12.30 p.m. Premedication consisted of 20 mg papaveretum and scopolamine 0.4 mg.

2 p.m. Chlorpromazine 50 mg, promethazine 50 mg and pethilorfan 50 mg were given slowly intravenously in a dilute solution over a period of 20 minutes. This made the patient drowsy, but he was still capable of answering questions.

2.25 p.m. Sleep was induced with thiopentone 250 mg followed by suxamethonium 50 mg, after which the lungs were inflated with oxygen. The pharynx, larynx and trachea were sprayed with 4 per cent lignocaine and a size 10 Magill orotracheal tube passed easily under direct vision. Spontaneous respiration returned in a few minutes but the patient resented the presence of the endotracheal tube and tried to remove it. Anaesthesia was maintained on a Magill semi-open circuit with nitrous oxide (6 l./min) and oxygen (2 l./min) and an additional 250 mg of thiopentone was given by intermittent injection before the patient settled.

The operation proceeded uneventfully and bleeding was slight throughout. The only untoward effect was a tachycardia of 100/min during handling of the gland. The blood pressure remained steady throughout; the lowest recording being 100/75 mm Hg.

4.10 p.m. Operation completed; B.P. 100/75 mm Hg, pulse 88/min. Pharyngeal and tracheal suction were carried out, the endotracheal tube removed and it was seen that both vocal cords were active.

8 p.m. Patient still unconscious. B.P. 130/75 mm Hg, pulse 136/min.

11 p.m. He was awake but still drowsy. B.P. 130/80 mm Hg, pulse 136/min.

4.9.58. 10 a.m. He complained of numbness and tingling in his right hand. On examination he was found to have gross muscle weakness of both arms and legs. He was unable to raise any of his limbs from the bed, nor was he able to produce flexion or extension at either the elbow or knee joints. Voluntary movements of the fingers and toes were also absent. There was no loss of sensation in any part of the body. The plantar reflexes were extensor. Left-sided ptosis was evident, the voice was weak and there was difficulty in swallowing. Despite this the respiratory muscles appeared to be unaffected by the paralysis and examination of the chest showed full and adequate expansion with no moist sounds on auscultation. B.P. 130/85 mm Hg, pulse 130/min.

At this stage it was thought that the weakness of the limbs might be due to the phenothiazine drugs which had been administered as part of the anaesthetic and improvement was expected to be rapid.

3 p.m. His condition was unchanged as regards the muscle weakness but he was now incontinent of urine. B.P. 130/85 mm Hg, pulse 140/min. The possibility of a thyrotoxic crisis with gross muscle weakness was

now considered and 10 ml of 0.4 per cent collosol iodine given without improvement. 11 p.m. The ptosis of the left eyelid made one think of the possibility of myasthenia gravis and atropine 0.6 mg followed by neostigmine 2.5 mg were given intravenously. This produced no improvement. Potassium chloride 0.5 g. was given and repeated 4-hourly by mouth to try and exclude the possibility of familial periodic paralysis.

5.9.58. His condition was unchanged. The flaccid muscle weakness was still present in both arms and legs but sensation remained intact. The ptosis of the left eyelid persisted and he had weakness of his voice and difficulty in swallowing. His serum potassium was 4.5 m.equiv/l. The urine contained no porphyrins.

Over the next few days there was a slight improvement in his condition, the voice became stronger and the difficulty in swallowing disappeared. A dramatic improvement did not occur, however, despite continuation of the potassium therapy and repeating the neostigmine on several occasions.

12.9.58. Myotonia was seen to be decreasing in his arms and he was able to grasp weakly with either hand. The improvement was more marked on the left side.

Repeated daily examination of the urine still revealed no porphyrins and there were no marked fluctuations in the serum potassium level.

20.9.58. The patient was now able to feed himself. His legs were becoming stronger and he was able to raise them a short distance from the bed.

5.10.58. Attempts at walking were made with the aid of the nursing staff and the weakness in the arms had almost completely disappeared.

20.10.58. He was now able to walk unaided, but he still complained of weakness after slight exertion.

During the past few weeks repeated examinations of his nervous system failed to reveal any abnormality other than the muscle weakness and diminished reflex activity. There were no signs of sensory disorder.

28.10.58. He was discharged from hispital feeling well except for weakness in his legs.

When seen three months after operation he stated that he felt well. There was no signs or symptoms suggestive of thyrotoxicosis and the muscle weakness had all disappeared.

DISCUSSION

Several different diagnoses were considered during the postoperative period.

It was thought that some of the drugs administered during anaesthesia might have been responsible for the muscle weakness. The most potent in producing a reduction in muscle tone are the phenothiazines of which chlorpromazine and promethazine were given immediately prior to operation, each in doses of 50 mg. Burn (1954) states that such dosage can produce a profound reduction in muscle tone. If a patient should be hypersensitive to the action of the drugs a syndrome such as presented in this case might have resulted. The phenothiazines are detoxicated and excreted fairly slowly from the body, but the length of time for which the muscle weakness persisted in this case would far exceed the duration of action of these compounds.

Porphyria was immediately thought of as a possible cause of the condition. Such cases show a marked sensitivity to barbiturates (Dundee and Riding, 1955) and administration of thiopentone can precipitate a fatal paralysis due to acute demyelinization of the nerve fibres. In many of the reported fatalities there was little to suggest the diagnosis of porphyria before operation, and for this reason the urinary investigations were frequently repeated, but negative results were obtained.

Familial periodic paralysis is a condition known to be associated with thyrotoxicosis (Weisman, 1952). It is rare in Europeans, but more common in Far Eastern subjects (Okinaka et al., 1957). The paralysis or muscle weakness is precipitated by the ingestion of a large quantity of carbohydrate and responds dramatically to potassium administration (Collings and Liendhart, 1957). This patient's illness was not made worse by carbohydrate in the diet, nor did it respond to potassium therapy. His blood potassium remained within normal limits during the first two weeks of his illness.

Myasthenia gravis is sometimes found as a complicating illness of thyrotoxicosis (Brain, 1940) and indeed the ptosis of the left eyelid and weakness in swallowing and phonation were very suggestive in this case. He did not, however, show any resistance to suxamethonium as has been shown by Churchill-Davidson (1955) to occur in patients having this disease. Failure to improve following neostigmine rules out this diagnosis.

Trauma to the cervical vertebrae with involvement of nerve roots in this region was also considered, but the type and distribution of the

muscle weakness together with the absence of sensory changes excluded this condition.

Poliomyelitis: clinically this illness did not resemble that of a true lower motor neurone paresis, and the distribution of the affected muscles was also against it being a likely cause.

Since this illness does not fit exactly into any of the clinical syndromes mentioned above, hysteria had to be considered. The patient was concerned about his helplessness and made great efforts to speed his recovery, whereas the opposite is usually characteristic of the hysterical patient. The classical sign of sensory loss not corresponding to anatomical nerve distribution was not found to support this diagnosis.

It will be apparent to readers that a definite diagnosis was not made in this case. Muscle weakness is an accepted symptom of thyrotoxicosis, but Brain (1955) considers that acute thyrotoxic myopathy is a very rare condition. The muscle weakness usually involves the muscles of mastication and there is generalized weakness of the limbs. It is usually associated with a thyrotoxic crisis. Sheldon (1946) reports recovery after treatment with neostigmine and partial thyroidectomy. The present case does not quite tally with the reported description of thyrotoxic myopathy and the only sign of a thyrotoxic crisis was the tachycardia which could have been due to the phenothiazine derivatives. Hyperpyrexia and metabolic disorders were absent and the patient did not respond to intravenous iodine.

No obvious relationship can be traced between the patient's postoperative condition and either anaesthesia or the conditions known to be associated with thyrotoxicosis. Hysteria is the only diagnosis which cannot be specifically excluded on the grounds of clinical examination or failure to respond to therapy. Whether this was in fact the cause of the weakness is very much open to speculation.

SUMMARY

A case of severe muscle weakness following thyroidectomy is presented. The differential diagnosis is discussed.

ACKNOWLEDGMENTS

I would like to express my thanks to Dr. R. G. Vine and Mr. H. M. Bennett for their permission to publish this case, and to Dr. J. W. Dundee for his help in preparing the manuscript.

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Brit. J. Anaesth. (1959), **31**, 459

THE INFLUENCE OF PYREXIA ON THE SIGNS OF SHOCK

BY

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THE way in which co-existent pyrexia may alter the classical picture of shock is not specifically described in the literature on the subject although the Medical Research Council Memorandum on the Treatment of Wound Shock (1957) does describe a variation of the shock syndrome seen in hot climates. The following case illustrates such an atypical picture as seen in a patient suffering from perforation due to diverticulitis of the colon with accompanying pyrexia.

Case History.

A man of 60, whose bowels had not moved for three days, complained of the sudden onset of generalized abdominal pain at 11.30 a.m. At the same time he felt cold and had a series of shivering attacks. He was seen at 3 p.m. by his family doctor whose findings were as follows:

Temperature 103.2°F; pulse rate 84/min; blood pressure 160/80 mm Hg.

Heart sounds were of good quality with no added sounds.

Respiratory system: nothing abnormal discovered.

Abdomen: tumid with generalized tenderness and guarding; no loss of liver dullness detected.

The patient gave a history of having had three severe attacks of coronary thrombosis during the previous ten years. However, these attacks had all the typical features of that disease and differed completely from the present illness.

The patient was seen again at 7 p.m. when the blood pressure was 120/80 mm Hg. There was loss of liver dullness. A diagnosis of a perforated viscus was made and the patient admitted to hospital where a straight X-ray of the abdomen revealed the presence of gas under the diaphragm. At 9 p.m. the patient was admitted to the ward where the blood pressure was found to be 70/55 mm Hg. This sudden and severe drop was thought to have been brought about by the ambulance journey and the manipulations in the X-ray department. An intravenous drip of 10 per cent dextrose in saline was started; 100 mg of pethidine were given intramuscularly and the decision was made to perform a laparotomy as soon as the patient's condition permitted.

I first saw the patient at 11 p.m. His temperature was still 103.2°F. I found him to be a well-built man of ruddy complexion, mentally alert with a pulse clearly palpable at a rate of 84/min. The capillary refill time was rapid. There was no suggestion of cyanosis of the skin which was warm and dry. The blood pressure was 60/50 mm Hg but the patient's general appearance gave a completely false impression belying the seriousness of his condition.

The intravenous drip was changed to dextran and blood was taken for grouping and cross-matching. By midnight the blood pressure had risen to 100/60 mm Hg, and it was thought that his condition would improve little more.

After the patient had been premedicated with atropine sulphate 0.6 mg, anaesthesia was induced with halothane and oxygen. A cuffed oral endotracheal tube was passed and the anaesthesia continued with the same mixture. A closed circle circuit with carbon dioxide absorption was used, the halothane being vaporised by the basal oxygen flow from the trichloroethylene bottle on the top circuit. The peritoneal cavity was full of faeculent fluid together with large quantities of solid faeces. No perforation in an area of diverticulitis of the colon could be found and the abdomen was closed with a transverse colostomy through the incision. The blood pressure had been maintained at 100/60 mm Hg during the operation and the patient was conscious on leaving the theatre. On return to the ward his blood pressure again started to fall and did not respond to further intravenous therapy. The patient died at 3 a.m.

DISCUSSION

If a human subject is strapped to a tilting table and changed from the horizontal to the vertical position, pooling of the blood occurs in the lower limbs. The faint which can occur may be delayed by reflex vasoconstriction of the vessels of the lower limbs. If the same experiment is repeated with an increased external temperature fainting occurs sooner, because the compensatory vasoconstriction in the lower limbs is prevented by the vascular mechanisms of temperature regulation (Wright, 1952).

The Medical Research Council Memorandum on the Treatment of Wound Shock (1957) describes how the classical picture of shock—pale, cold, sweating and probably slightly cyanosed skin, together with low blood pressure and rapid pulse—may be modified in hot climates to one of "warm hypotension"—warm extremities, pale or well coloured face, low blood pressure and rapid pulse.

Similarly it seems reasonable to expect that a co-existent pyrexia might modify the signs of shock and the above case confirms this.

Patients suffering from both severe shock and pyrexia are not commonly seen, but accurate assessment of their state is essential for the proper choice of the method of anaesthesia. Measurement of the blood pressure at frequent intervals is necessary as the external appearance and pulse may be quite misleading and the degree of shock may increase considerably without obvious change in the external appearance. In choosing a method of anaesthesia it must be remembered that the pyrexia deprives the patient of a varying proportion of the reflex vasoconstrictor response to fall in blood pressure and any anaesthetic drug or technique which may cause such a fall in blood pressure should be avoided.

ACKNOWLEDGMENT

I am grateful to Mr. T. F. R. Griffin for permission to publish details of this case.

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MANCHESTER MEDICAL SOCIETY

Section of Anaesthetics

1959	
October 15.	Presidential Address: "50 years of Anaesthesia."
November 26.	Dr. V. Keating: "The Metabolic Reaction to Surgery in coloured patients."
1960	
January 28.	Registrars Meeting: Dr. I. Hallack. Dr. B. J. Muir.
February 25.	Symposium on Dental Anaesthesia: Dr. T. Dinsdale. Dr. W. Ken Jones. Mr. G. Ashcroft.
March 31.	Dr. Frankis T. Evans: "Mistakes I have made."
April 28.	Joint Meeting with the Liverpool Society of Anaesthetists at Manchester. Dr. G. N. Mulliner: "Anaesthesia and Body Temperature." Dr. J. C. Richardson: "New Developments in Anaesthesia for Cardiac Surgery."

Brit. J. Anaesth. (1959), **31**, 461.

AN INTERESTING CASE OF RECURARIZATION

BY

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THE relatively short duration of the clinical action of curare given intravenously results from the distribution of the drug through the extravascular compartment. The concentration of curare in the plasma falls rapidly, to a point below that required to produce overt muscular paralysis, although up to 25 per cent of the initial plasma concentration of curare may be detected in the blood 1 hour later (Cohen et al., 1957; Pittenger et al., 1951; Marsh, 1951). Renal excretion and metabolic destruction of the drug are relatively slow processes and have been shown to be continuing 24 hours after the injection of a paralytic dose of d-tubocurarine chloride (Marsh, 1952).

Due to the prolonged presence of the active compound in the body, recurarization is possible. Following the use of antidotes such as edrophonium or neostigmine to treat residual curarization, the effect of the antidote may wear off before the plasma curare level has fallen below that concentration which producess obvious muscular weakness (Doughty and Wylie, 1952; Foldes et al., 1952). The occurrence has been discussed by Spears (1951).

There are two other possible causes of recurarization. Marsh (1952) suggested that a sudden gross postoperative loss of electrolytes and fluid might result in a displacement of curare from extravascular sites into the circulation. As the extravascular compartment may hold as much as half of the injected curare, recurarization may occur. The other possible cause is an enhanced sensitivity of the myoneural junction to curare during the postoperative period. This would cause paralysis at a plasma curare concentration previously too low to cause obvious weakness. Foldes (1957) suggests this may occur as the result of a postoperative reduction in the plasma potassium concentration. The case reported below is of interest as it substantiates this latter possibility. The main cause of recurarization was an increasing sensitivity to curare at the myoneural junction, due to a fall in the serum potassium level.

CASE REPORT

The patient, J. A., aged 71 years, was operated upon on November 5, 1958, for resection of atheromatous aneurysm of the abdominal aorta extending from 1 inch below the origins of the renal arteries to the bifurcations of the common iliac arteries on both sides. The excised portion of the aorta was replaced by a homograft.

Pre-operatively the patient was grossly underweight, weighing 6 stone 5 lb. (40 kg). This was attributed to a long history of duodenal ulceration for which a partial gastrectomy had been performed 8 months previously. He gave a history of a "coronary thrombosis" in 1955. His e.c.g. showed changes suggestive of an old small posterior myocardial infarct. His pre-operative haemoglobin, electrolytes and blood urea were within normal limits. A radio-active chromium tagged red cell blood volume estimation showed that on the morning of the operation his circulating blood volume was 3.34 litres.

The patient was premedicated with pethidine 50 mg and atropine 0.65 mg. Anaesthesia was induced with 300 mg of thiopentone. Following suxamethonium 50 mg, intubation was performed using a no. 9 Magill endotracheal tube. When spontaneous respiration had returned d-tubocurarine chloride, 15 mg, was given, but a further 10 mg was required to obtain complete relaxation. Manual intermittent positive pressure ventilation was maintained with 2 litres per minute of oxygen and 5 litres per minute of nitrous oxide in a semiclosed system. Anaesthesia progressed satisfactorily. Intermittent doses of pethidine 10–15 mg and of d-tubocurarine 5–7 mg, were given at the first signs of returning respiration. The soda lime canister was changed after 4 hours continuous use.

The operation progressed well until after the graft was in place and the proximal clamps loosened. At this point torrential haemorrhage occurred through a defect in the graft which necessitated the infusion of 1,600 ml of blood in 10 minutes. The defect was repaired but, due to persistent oozing of blood from the retroperitoneal tissues, the operation became protracted. Ten ml of 10 per cent calcium gluconate solution were given for every 3 bottles of blood infused, but the blood loss continued. This was later shown to be due to an excessively low plasma fibrinogen level.

The operation ended 8¼ hours after induction of anaesthesia. A total of 67 mg of d-tubocurarine

chloride had been administered during this period. At this time the patient's nasopharyngeal temperature was found to be 36.5°C. Spontaneous breathing occurred readily on allowing some accumulation of carbon dioxide but, in view of the large dose of curare administered, atropine 0.6 mg was given, followed by neostigmine 2.5 mg. The patient was breathing well; he had active reflexes and would open his eyes on command. A total of 5,130 ml of citrated blood had been infused and a blood volume estimation at this time showed a deficit of 0.63 litres. This was the magnitude of the error resulting from swab weighing.

The patient was fully conscious on return to the ward and his condition remained good for 3 hours, when he suddenly showed signs of internal haemorrhage. Further blood was given and preparations were made to explore the site of the graft.

The second anaesthetic lasted a little under 5 hours, during which time a further 20 mg of d-tubocurarine chloride was administered. The operation revealed no specific bleeding point but rather a generalized ooze of blood. Infusion of 500 ml of quadruple strength plasma and 25 g. of fibrinogen lessened the bleeding to a degree that was considered safe after which the abdomen was closed. At this time 9,720 ml of stored blood had been administered and the blood volume was estimated to be 0.53 litres below the pre-operative level. At the end of the operation atropine 0.6 mg was administered, followed by neostigmine 2.5 mg. The patient was returned to the ward awake, co-operative and with active reflexes.

The condition of the patient remained satisfactory for 3–4 hours. He then slowly became progressively weaker and his respiration became depressed. When seen 5 hours after the end of the second operation he was comatose and cyanotic. His respirations were gasping and associated with a pronounced tracheal tug. The trachea was intubated with ease and a sample of alveolar carbon dioxide was taken using a rebreathing technique. Gas analysis with a Drager carbon dioxide analyzer, gave results of 10 per cent and 10.5 per cent. Hyperventilation through a soda lime canister for 10 minutes produced a considerable improvement in the patient's condition, and his level of unconsciousness lightened so that he became intolerant of the endotracheal tube. This confirmed the diagnosis of carbon dioxide retention coma. After removal of the endotracheal tube, the patient again lapsed into coma. Re-intubation was performed and the hyperventilation repeated. It was observed that there was little resistance to artificial ventilation and the possibility of recurarization was therefore considered. Edrophonium 10 mg was given with dramatic effect; the patient started breathing deeply and in a few minutes he had regained consciousnss and removed the endotracheal tube. The improvement lasted about 7 minutes, when respiratory weakness returned. Atropine 0.6 mg was given, followed by neostigmine 2.5 mg.

Again the response was dramatic and within a few minutes the patient was moving about in his bed complaining of abdominal pains. The possibility of hypokalaemia as a contributory factor was considered at this point in order to explain the considerable delay in the onset of recurarization. Serum and urine electrolyte studies were performed. The serum potassium had fallen to 3.4 m.equiv/l. and the urinary potassium concentration had reached 66 m.equiv/l. with a total urinary output of 982 ml in that day.

The effect of the neostigmine lasted long enough to cover the period of recurarization. Twenty-four hours later the continuing hypokalaemia had become obvious as a separate clinical entity, manifesting itself as drowsiness, lethargy and mental confusion. The alveolar carbon dioxide was within normal limits. At this time the serum potassium concentration was 3.0 m.equiv/l. Intravenous infusion of potassium chloride corrected the plasma potassium deficiency which correlated with improvement in the patient's condition. By the fifth postoperative day, the urinary output potassium had fallen to 29 m.equiv per day and the patient was quite well. Unfortunately, in spite of continued good progress the patient suffered a cerebral vascular accident and died on the eleventh postoperative day. The postmortem examination showed recent multiple cerebral infarcts, presumably due to multiple emboli.

DISCUSSION

There were several factors of interest in this case:

(1) The patient was initially grossly underweight as a result of his previous illness. It would therefore be expected that his total body potassium would be abnormally low.

(2) Over the course of the two operations he received transfusion of 18 bottles (9,720 ml) of "Acid Citrate Dextrose" (A.C.D.) blood. This blood is known to have a high potassium content, which is estimated to be in the region of 50 to 60 m.equiv/l. after 10 to 14 days (Loutit et al., 1943). Estimation of the patient's blood volume by means of radioactive chromium tagged red blood corpuscles showed that after the first 5,400 ml of blood had been infused only 22 per cent of the patient's red corpuscles were his own. It is probable that the majority of the patient's plasma was also derived from the donor blood and therefore a high serum potassium would seem inevitable. The raised serum potassium would have been accentuated by the second operation and the infusion of a further 4,320 ml of stored blood.

(3) A total of 87 mg of d-tubocurarine chloride was administered during the two operations over a period of 16½ hours. The actual operating time was 13 hours. It is possible that the raised serum potassium induced an artificial resistance to the action of curare (Wilson and Wright, 1937) and necessitated the administration of a large total dose of the drug, much of which would be deposited in the extravascular compartment.

(4) Following the end of the second operation there was a large renal excretion of potassium, partly as a result of the high plasma level and

partly as a response to the stress of operation. Associated with this renal loss, potassium may have entered the cells as a result of pre-existing depletion and this would be aggravated by infusion of 5 per cent dextrose in water during the 22 hours which preceded the establishment of the recurarization. In these circumstances the myoneural junctions would be increasingly sensitive to the effect of the residual curare and recurarization would occur.

SUMMARY

This case presents an unusual and dramatic example of recurarization due probably to an increasing sensitivity of the myoneural junction associated with a fall in the plasma potassium concentration. Due to the circumstances of this case the recurarization and its response to antidotes was most dramatic. It is possible that, as the result of a fall in plasma potassium, some degree of recurarization may occur in any patient to whom a large total dose of d-tubocurarine had been administered. This may be due to the metabolic response to stress, the infusion of dextrose, the repletion of pre-operative intracellular deficiency or to the administration of large doses of adrenal corticoids postoperatively. The presenting clinical picture may show merely weakness of the ocular muscles, or difficulty in swallowing, or rarely, as in this case, the appearance of marked respiratory paralysis.

ACKNOWLEDGMENT

I would like to thank Sir Stanford Cade, Dr. R. Machray and Mr. C. Westbury for permission to publish this case.

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Brit. J. Anaesth. (1959), **31**, 464

A RESTATEMENT OF ANAESTHETIC PRINCIPLES

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FOR some twenty years prior to the introduction of the muscle relaxant drugs, the development of anaesthesia was characterized by increasing complexity of technique and apparatus. To ensure the best possible operating conditions for the surgeon, together with the least toxic combination of drugs for the patient, the anaesthetist had to be highly versatile. The scope of anaesthesia was being extended in many directions, and often the facilities for accurate physiological measurement in the operating theatre were not available. Under these conditions, it was often an "advance" to provide an anaesthetic method which would enable the operation to be completed without inflicting too much harm on the patient.

Since the introduction of the muscle relaxant drugs, several moves have been made towards a resimplification of clinical anaesthesia (Nosworthy, 1953; Macintosh, 1955). Many of the more difficult, time-consuming and elaborate techniques have been relegated to positions of comparative insignificance. At the same time, many of the skills necessary to the anaesthetist of a previous generation have been rendered superfluous by the facility with which the difficult procedures of the past can now be bypassed. Furthermore, whereas the anaesthetist formerly had to choose which of several potentially toxic combinations of drugs would be the most suitable to a particular patient or for a particular operation, the anaesthetist is today in the position of being able to use combinations of drugs in dosages which are virtually innocuous to the patient whatever his condition may be, or whatever operation it is proposed to undertake. It is not surprising, therefore, that many of the classical indications for choice of a particular anaesthetic technique have ceased to exist.

Although this resimplification of anaesthesia has effected considerable changes, with evident benefit to the patient, many of our current practices still represent a hangover from the past. Anaesthesia has made great progress, and the time has now come to consider how much of our inheritance is superfluous, outdated, and needlessly unscientific. Having done this, it should be possible to envisage the essential requirements for safety and up-to-date usefulness. From this basis, by adding such refinements as are dictated by circumstance, it should be possible to develop a simple concept of anaesthesia which would eliminate most of the uncertainty and superstition that have grown up in the past.

CHOICE OF TECHNIQUE

This difficult problem has been discussed previously, and the pitfalls involved in the application of statistical conclusions to individual cases have been stressed (Parkhouse, 1957). A study of anaesthetic practice in different centres shows quite clearly how little general agreement there is concerning the value of different methods. In the United States, the Magill semi-closed system (the traditional "top circuit" of the Boyle machine) is almost unused. In most places a circle system is employed for every case, respiration being assisted or controlled whenever an indication is felt to exist. It is perhaps pertinent at this point to mention the popular belief that a closed circuit is essential for thoracic anaesthesia; even the latest edition of a well-known book perpetuates this myth (Beecher, 1958). As long as the patient's respiration is controlled, the closed system offers no possible advantages over the nonreturn. The latter, in fact, offers attractions which will be further referred to below.

Ayre's T-piece is another example of the empiricism which surrounds the question of anaesthetic method. When first introduced, this purported to be one of the simplest means of anaesthetic maintenance, and yet it has proved to have mathematical and physical characteristics which defy all attempts at calculation. Despite many variations of the T-piece, speculation still runs high as to what flowrate of gases is required relative to any particular length of tubing, in order to ensure adequate elimination of carbon dioxide. In clinical practice, the claims made for the T-piece still result from supposition rather than fact. In the field of neurosurgical anaesthesia, for example, some skilled and experienced anaesthetists favour the T-piece, while others use the so-called semi-closed system. It is unlikely that most enthusiasts could produce a single piece of factual evidence for or against the method of their choice; their cases do equally well.

Neurosurgical anaesthesia has long been a stronghold against controlled respiration. For years we have been told that intermittent positive pressure ventilation during neurosurgical anaesthesia will raise the cerebrospinal fluid pressure, increase bleeding and hamper the work of the surgeon. Here again the statements have been the result of guesswork rather than investigation, and there is now good reason to believe that the opposite is true (Galloon, 1959; Mortimer, 1959). Many other examples could be given where the anaesthetist's choice is determined merely by habit, prejudice or pseudoscientific speculation. Enough has already been said, though, to bring out the point that the accepted indications for particular anaesthetic methods have little scientific backing, and have never been brought into line with the changing outlook of modern anaesthesia.

SHORTCOMINGS OF TECHNIQUE

Whichever of the conventional closed or semi-closed methods is finally selected, it will suffer from the disadvantage of not having been designed to facilitate measurement. The composition of the inspired gas mixture, for example, is usually unknown. Although it may be possible by the use of complex scientific apparatus to collect valid gas samples and discover retrospectively what the patient was breathing, and although it may be diverting for the mathematical physicist to relate these practical discoveries to his theoretical calculated values, such procedures are always likely to be outside the scope of the practising anaesthetist. In any case, the introduction of a non-return valve obviates the necessity for such measurements and calculations. Again, practically none of the apparatus in current use has provision for the quantitative administration of anaesthetic vapours. It is deplorable that after more than 100 years of anaesthetic progress, fatalities can still occur because the patient "probably" or "almost certainly" received a dangerously high concentration of a volatile agent. These concentrations should be known (Edwards et al., 1956).

Several other sources of error exist. There are numerous points at which a complex anaesthetic circuit can leak. The conventional shape of the anaesthetic bag makes for difficulty in measuring tidal volume. When the bag is squeezed about its middle, some of the content is expelled towards the patient while an unknown amount passes back into the distal end of the bag which becomes more distended. The corrugated anaesthetic tubing in common use is also distensible, and adds further to the difficulty of knowing how much gas reaches the patient's lungs (Dobkin, 1958). The use of the "near-closed" circuit, or "spill-over" technique, in which the patient is ventilated through a circle system with a Heidbrink valve left partially open, introduces a further uncertainty. With this method it is impossible to tell how much gas passes into the patient and how much spills out into the operating theatre. Should the compliance of the lungs suddenly change as a result of the surgeon's manipulations, it may well be some time before this alteration is adequately appreciated by the anaesthetist, since when he now squeezes the bag the only change is that a little less gas passes to the patient and a little more out of the valve. All these factors combine to make the estimation of tidal and minute volume so difficult that most clinical anaesthetists do not know within very wide limits what gas volume they are delivering to the patient. There is much glib talk of hyperventilation and hypoventilation, and much discussion of blood CO_2 levels, but little reliable data from which cause and effect can be correlated.

When these facts are considered, we may well pause to ask whether it is worth while burdening

the minds of juniors with so many different circuits and arrangements, when one would suffice. We might go further, and ask ourselves whether it is worth our own while concerning ourselves so much with the applicability and efficiency of various different methods of anaesthesia, when we could more profitably be devoting our attention to the patient's welfare. When one is thoroughly conversant with a single method, and has used it many thousands of times, it becomes second nature to use it competently and effectively. Changes in the patient's condition are then far more readily appreciated.

THE CHOICE OF DRUG

Pride of place must be given among the anaesthetic agents, as far as current practice in this country is concerned, to nitrous oxide. Nitrous oxide has long been recognized as a nontoxic agent, and since the introduction of the muscle relaxants it has come into its own because its relative lack of potency is no longer a serious disadvantage. Ether, on the other hand, has an evil reputation as far as toxicity is concerned, and this is largely attributable to the fact that in the days when muscle relaxants were not available, ether was the drug principally used when deep anaesthesia was required. All anaesthetic agents are toxic when used to produce deep anaesthesia, and it is unreasonable that the reputation of ether in this respect should be allowed to persist. In fact, when 2–4 per cent of ether vapour is administered to a patient, he will be awake and talking at the end of the operation just as if he had been given nitrous oxide, and recent carefully controlled studies (Dobkin, 1959) tend to support the commonsense view that all anaesthetic agents are equally harmless in equipotent small doses. When muscle relaxants are available, so that the quantities of general anaesthetic can be kept to a minimum, it is probably of rather small significance which agent is chosen. In these circumstances one of the most important considerations is ease of administration, and in this respect nitrous oxide is at a grave disadvantage.

The use of medical gases, which have to be specially prepared, purified and dried, presents many problems, particularly in remote countries. It is not suggested that we should modify our anaesthetic techniques merely because people in other parts of the world do not enjoy all the opportunities we do, but quite apart from this it seems needless to resort to using artificial mixtures of gases when nature has provided us with an atmosphere containing enough oxygen for our requirements. The use of cylinders in the operating theatre involves the anaesthetist in a constant vigil to ensure that the gases do not become exhausted. When a cylinder does have to be changed, this involves an interruption in his administration of the anaesthetic, it involves noise which may be disturbing to the surgeon, and it may even necessitate the anaesthetist leaving the operating theatre in order to bring in a fresh supply. When the full cylinder is brought in, possibly from the hospital backyard, it may be covered with dust and dirt. Apart from bulkiness and weight, gas cylinders add tremendously to the size and complexity of our anaesthetic apparatus by necessitating the use of reducing valves, flowmeters, and other paraphernalia.

The use of artificial gas mixtures for anaesthetic maintenance involves a complete alteration of the gaseous physiology of the body. The necessity for denitrogenation before effective nitrous oxide anaesthesia is well known, and some anaesthetists now add as a further requisite, pre-oxygenation. At the end of the operation, nitrous oxide has to be eliminated, with the possibility of diffusion anoxia (Fink, 1955). This type of alteration of the patient's basic physiology introduces unnecessary complications, since it is perfectly feasible to maintain anaesthesia with air. This situation is rather analogous to the problem of maintaining the electrolyte and nutritional balance of the patient by means of intravenously administered fluids. The introduction of sodium chloride infusion was a major advance in therapy, but when the additional problems concerned with the metabolism of other electrolytes, and with the maintenance of body weight and full dietary requirements are taken into consideration, it becomes extremely difficult to provide an adequate long-term alternative to natural feeding. Although remarkable therapeutic triumphs have been achieved, most physicians still agree that the best thing for a patient is to re-establish normal feeding by mouth at the earliest possible moment. In passing, it should be pointed out that by interfering with the standard physiological methods of

gas analysis, the use of nitrous oxide has stood in the way of certain aspects of anaesthetic research for many years.

PRESENT-DAY REQUIREMENTS

Although it has been suggested that inhalational anaesthetic agents are destined to lose their place in the future (Armstrong Davison, 1958), they still offer considerable advantages. The non-reactive nature of these agents, together with the ease with which minute-to-minute adjustments can be made in the concentrations delivered to the patient, make for a degree of versatility which is unique, and most anaesthetists would agree that an anaesthetic apparatus without provision for delivering such agents to the patient would be, to say the least, incomplete. However, unless the apparatus for administering these agents is capable of delivering known and consistent concentrations, something much less than perfection has been achieved. Simple and reliable quantitative inhalers are currently available. Since the original description of the E.M.O. inhaler (Epstein and Macintosh, 1956), this apparatus has been modified and calibrated for use with trichloroethylene, halothane, and the halothane-diethyl ether azeotropic mixture, so that any of these agents can be administered quantitatively. Calibration is also possible for any other agent which may come into use. Such inhalers enable room air to be drawn over the selected volatile agent, so that known concentrations of its vapour in air are delivered to the patient. This is the simplest, most logical, and most reliable method of administering an anaesthetic. It is a method which has been in constant use in the Nuffield Department of Anaesthetics for many years, and has given complete satisfaction in many thousands of cases. More recently, other workers have begun to think along the same lines, and have designed apparatus of their own (Nandrup, 1959; *Lancet*, 1959).

A reliable means of inflating the patient's lungs must be available, and such an appliance can be used in conjunction with the inhaler. The Oxford Inflating Bellows (Macintosh, 1953) was designed for this purpose, and since then Ruben has described a self-filling bag which fulfills the same function by drawing air into itself through a nonreturn valve system. Each of these pieces of equipment is very satisfactory, although a bellows offers certain advantages over a bag. Firstly, it can rather more conveniently be connected to an inhaler. Secondly, its shape enables a more accurate estimation of the tidal volume to be made. Thirdly, by virtue of its relatively inelastic characteristics, the bellows makes it easy to appreciate small changes in resistance to ventilation. A further advantage is that the bellows can very simply be mechanized, as in the well-known Radcliffe series of pumps, to make a mechanical respirator (Russell et al., 1956). Provision is also made, both on the bellows and on the Ruben bag, for the addition of extra oxygen should this be deemed necessary.

The anaesthetic apparatus can now be completed by adding a piece of wide-bored tubing (preferably nondistensible) leading to the patient. Since a nonreturn valve is incorporated in the bellows, a standard expiratory valve at the face mask or endotracheal tube connector will ensure that the patient inspires the mixture that is delivered from the inhaler, and that all his expirations pass into the operating theatre. For controlled respiration, the standard expiratory valve may be replaced by an inflating valve such as the one described by Mitchell (1959). Alternatively, the nonreturn valve of the bellows unit may be immobilized by means of the magnet provided, and a Ruben valve may be used at the face instead. In this way a simple nonreturn system is provided whether the patient's respiration is spontaneous or controlled. This complete anaesthetic arrangement is not only simple and easily portable, but is applicable to all the circumstances of clinical practice. It offers a single reliable arrangement which can be used for every case, comprising the minimum number of mechanical appliances that can give trouble, and offering the anaesthetist the least possible distraction from his patient. When the inhaler and the bellows have been used sufficiently often for confidence to be acquired the advantages of consistent reliability become apparent to the anaesthetist.

One further addition to the equipment outlined, which might be regarded as a kind of "optional extra", is a dry gas clock which can be connected by means of a piece of corrugated tubing to the expiratory side of the Ruben valve.

With this addition, it becomes a simple matter for the anaesthetist to monitor the patient's ventilation.

ADVANTAGES OF AIR

Apart from dispensing with cylinders, reducing valves, flowmeters and humidifiers, the use of atmospheric air as a vehicle for inhaled vapours offers positive advantages both to the patient and the administrator. However, anaesthesia has become such a sophisticated specialty that any suggestion that air, without additional oxygen, is adequate for anaesthetic maintenance is liable to be greeted with suspicion and frank disbelief. With the liquid anaesthetics in common use, the quantity of vapour required for the maintenance of light anaesthesia makes only an insignificant difference to the percentage of oxygen in the inspired air, and an unconscious patient immobile on the operating table can be fully oxygenated with this mixture. Although it has been suggested (Cullen et al., 1956) that under anaesthesia ventilation must be two or three times the normal resting volume in order to ensure adequate clearance of carbon dioxide, this is manifestly untrue. It is a well-established fact that completely paralyzed patients can be maintained on intermittent positive pressure ventilation with air alone for many months without adverse effects. Such patients, in fact, invariably show low CO_2 levels even if only moderately hyperventilated. In clinical anaesthesia, anoxia rarely occurs as an isolated event. It is commonly due to inadequate ventilation, the result of either respiratory depression or respiratory obstruction, and it is consequently associated with carbon dioxide retention. If a patient is breathing room air and is not ventilating his lungs adequately, cyanosis results, and recent studies have suggested (Scurr, 1956) that this cyanosis becomes evident at a time when the blood level of carbon dioxide is approximately twice the normal. Such a carbon dioxide level will not result in serious harm, and with the warning of cyanosis, the anaesthetist's attention is drawn to the necessity for increasing ventilation by some means or other. If the patient is breathing an oxygen-rich mixture, it is an appreciable time before cyanosis becomes manifest, and this may lull the anaesthetist into a false sense of the patient's wellbeing. If the patient were to turn bright green when his blood carbon dioxide level rose to, say, 80 mm Hg, anaesthetists would be just as alarmed at this phenomenon as they now are by cyanosis, and they would feel equally obliged to take brisk action. The accurate determination of blood carbon dioxide levels is a complicated, time-consuming and suspiciously inaccurate procedure, and yet the routine employment of high oxygen concentrations in anaesthetic practice is the very reason why such measurements are essential. Indeed, much of the exaggerated importance that has been attached to carbon dioxide tensions in recent years has been a result of the fact that with conventional anaesthetic methods these tensions represent one of the very few indices of the adequacy of ventilation. Whenever arterial oxygen saturation measurements have been made on patients ventilated with air they have proved to be within normal limits, and a recent study (Nandrup, 1959) reveals that adequate ventilation with light ether and room air results in oxygen saturations equal to or higher than normal. It need hardly be added that air offers a uniquely constant composition mixture of gases already humidified to such a degree that prolonged administration is possible, even through a nonreturn system, without fear of detriment to the patient's lungs.

In thoracic anaesthesia, one's first instinct is to add oxygen to the inspired mixture in view of the fact that the lung is partially collapsed and may be retracted out of the surgeon's way. Once again, however, the problem is not exclusively one of anoxia, but of carbon dioxide retention as well, and the answer lies not so much in the addition of oxygen as in the institution of adequate ventilation. In any event, at least in the lateral position, much of the pulmonary blood flow passes through the dependent lung and, furthermore, blood passing through unventilated areas of lung will not be oxygenated even if the patient is inflated with pure oxygen. It is not intended to imply that there are no circumstances under which oxygen should be added to the inspired mixture, but it is worthy of note that Continental workers have observed that during thoracic anaesthesia a switch from open ventilation with air to closed circuit ventilation with oxygen produces no noticeable difference in the blood oxygen saturation (Poppelbaum, 1959).

THE ADVANTAGES OF THE NONRETURN SYSTEM

Some advantages of this type of system have been referred to already. It recommends itself because of its inherent simplicity, and because it frees the anaesthetist from dependence on soda lime and elaborate apparatus. It ensures that the patient receives a fresh supply of gases with each inspiration, and that the composition of the inspired gas mixture is accurately known.

Quite apart from these advantages, a nonreturn system has a distinct appeal on purely hygienic grounds. Whatever may be said about the self-sterilizing qualities of anaesthetic tubing, and however many negative bacteriological reports may have been obtained, there still remains something inherently distasteful in the thought of inhaling from tubing through which a previous patient has coughed. If the anaesthetist himself were invited to take a few deep breaths from a piece of anaesthetic tubing which a chronic bronchitic patient had just sprayed with particles of sputum it might be brought home to him that present standards of anaesthetic cleanliness are not all that they might be. Most anaesthetists engaged in thoracic work are in the habit of boiling or otherwise sterilizing their anaesthetic tubing after a tuberculous patient has been anaesthetized. This speaks for itself, and the confinement of this practice to those patients known to be tuberculous is a half-hearted gesture in view of the fact that many other cases are undiagnosed, and that there are, in any case, far commoner chest infections. With a nonreturn system, the only parts of the apparatus through which the patient can rebreathe are the endotracheal tube and its connector, and the valve. All of these can be sterilized between cases.

CONCLUSION

When simple methods for using air in anaesthesia were first introduced, they were, under many circumstances, the only methods available. Most people are prepared to admit that under field conditions and in backward communities such techniques are admirable, but it has never occurred to many people to consider the possibility that these same methods actually offer certain advantages over the ones they currently use. Now that the muscle relaxant drugs are available, satisfactory operating conditions can be provided by the use of nontoxic doses of volatile agents, the patient can be assured of an adequate airway by means of an endotracheal tube, and he can also be assured of adequate pulmonary ventilation. It would seem that the quantitative administration of volatile liquid anaesthetic agents in air, through a nonreturn system, is the logical method of anaesthesia for the present day. It is the method which assures constancy, and which by measurement eliminates as many as possible of the unknown factors in anaesthesia.

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BOOK REVIEWS

Resuscitation of the Unconscious Victim. By Peter Safar, M.D., and Martin C. McMahon. Published by Charles C. Thomas, Springfield, Illinois. Price 12*s.* 6*d.*

This is a manual for laymen. It needs to be simple. Simple books are the most difficult to write; but this one is very good.

The technique of artificial respiration advocated is "Mouth-to-mouth Breathing" on which Dr. Peter Safar has done so much work. However, there is nothing partisan about this book. It is enlightened throughout by the sort of sound sense which one expects from an anaesthesiologist. For example, see page 74: "We believe that the teaching of the 'head-tilt, chin-up' position will save more lives than the teaching of any method of artificial respiration". Look too, at the illustration on the cover, a rescue man, *supporting* the jaw and *looking* at the chest.

If you have to train rescue workers, you must read this book. The authors say, "It is probably advisable that each ambulance service establishes its own 'standard of procedures' . . .". Therefore there is bound to be some detail with which you will disagree. However, if the broad plan of the book fits reasonably well into your own "standard of procedures" you will have cause to be very grateful to these authors.

Evidently a great deal of thought has been given to the compilation. It would be possible to tear out whole chapters, or to score out and alter phrases, in order to fit the material to your own "standard of procedures" and avoid confusion in the pupil's mind, while still retaining a most valuable manual. One suspects that this is no accident.

E. A. Pask

Symposium on Pulmonary Ventilation. Edited by Dr. R. P. Harbord and Professor R. Woolmer. Published by John Sherratt and Son, Altrincham. Pp. 109; illustrated. Price 12*s.* 6*d.*

This volume records the papers and discussion at a meeting in Leeds University, organized by Dr. R. P. Harbord, under the auspices of the *British Journal of Anaesthesia.*

There are three papers mainly concerned with measurement, two upon problems arising in the treatment of emphysema, one upon the problems of the newborn, and one dealing with lung ventilation during hypothermia.

The fully recorded discussions serve to unite the contributors into a team, so that it would be wrong to select individual papers for attention. The material and ideas recorded will be of great interest and value to all thoughtful anaesthetists.

The full recording of discussion is interesting. On this occasion, speakers were given an opportunity to correct the record of their remarks. This seems to be the only feasible method; but when given this opportunity, one tends to correct the record toward that which one meant to say and it may not be quite what one *did* say, in the heat of the moment. In consequence, a colleague's recorded reply may be appropriate to what one actually said; but it may not seem quite appropriate to what one meant to say, and which now stands in the record. Readers must be wary of this; but, allowing for it, they will find the recorded discussions most interesting.

These ambitious editors are to be congratulated. It is a very workmanlike job and should not be missed.

E. A. Pask

Printed in Great Britain by JOHN SHERRATT & SON, Park Road, Altrincham